Complementary and Alternative Therapies

(CAM01)

Multiple Sclerosis Imbalance: Visual Rehabilitation

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Background: Imbalance is among the most debilitating symptoms in Multiple Sclerosis (MS), causing falls and reflecting, to a large extent, the dysfunctional integration of visual sensory signals.

Objectives: This preliminary study aimed to show the effects of visual rehabilitation on balance in a small group of people with MS.

Methods: Three people with MS presented signs and symptoms of body imbalance. All were evaluated before and after visual rehabilitation by specialized optometrist, from ocular motility, cover test and stereoscopy, as well as chromatic and pupil analysis. Rehabilitation consisted of 7 sessions involving balance exercises associated with vision.

Results: In the initial evaluations, participants presented the same pattern of body imbalance. After visual rehabilitation, improvements in body posture, static and dynamic balance, and overall physical performance were observed in all participants.

Conclusions: The data obtained revealed that visual function contributes positively to the postural control system and suggests that visual rehabilitation may be an advantageous option for the treatment of imbalance in MS, since it involves ocular exercises capable of producing physical and mental stimuli that, as they improve vision, make it possible to decrease the rates of falls and consequent impairment of functional capacity.

Disclosure: *Nothing to disclose.*

Keywords: Complementary/alternative therapies in MS

(CAM02)

Acupuncture and Electromagnetotherapy for Chronic PAIN Relief in Multiple Sclerosis

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Background: Chronic pain is common in people with multiple sclerosis (PwMS) with approximately 42% to 90% experiencing pain at some stage of the disease course. Pharmacological treatment in MS-related pain are usually unsatisfactory and often have severe side effects, and therefore, a need for alternative methods of pain relief is critical.

Objectives: To evaluate the effectiveness and analgesic efficiency of acupuncture associated with electromagnetotherapy for chronic pain relief in a PwMS group.

Methods: A total of 12 patients with multiple sclerosis were included in this prospective study, being 10 women and 2 men, aged between 40 and 74. Mean Expanded Disability Status Scale (EDSS) score was 4.8; 42% of patients were classified as having relapsing-remitting multiple sclerosis, 33% as secondary-progressive, and 25% primary-progressive. All complained of pain (10= back, 2= legs/feet), used pharmacological treatment, underwent 15 acupuncture sessions and electromagnetic therapeutic equipment applications (Kenkobio®), and answered a structured pain questionnaire.

Results: The primary end point was reduction in pain intensity or elimination, whilst the secondary end point improved symptoms and quality of life. This preliminary study revealed that MS-related pain can have a significant impact on health, activity, and participation. of people, drastically reducing the quality of life.

Conclusions: Although our overall results suggest that these non-pharmacological interventions had beneficial effects on chronic pain and were not harmful, studies with robust methodology are needed to assess safety and possible long-term effects, justifying the use of these interventions on chronic pain in MS.

Disclosure: *Nothing to disclose.*

Keywords: Complementary/alternative therapies in MS

(CAM03)

The Effects of Reflexology in People with Multiple Sclerosis

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Background: Multiple sclerosis (MS) is associated with a wide variety of different physical and psychological symptoms that have a profound effect on quality of life. Complementary and

alternative medicine (CAM) is a current treatment which seems is effective in relieving symptoms of patients with MS.

Objectives: To show the opinion of a group of people with MS about the effects of reflexology.

Methods: This study involved 12 people with MS and healthy feet without injury, damage, thrombosis, inflation, lesion, or fractures, 7 (58%) women and 5 (42%) men, aged 25 to 72 years and mean Expanded Disability Status Scale (EDSS) score 4.5. In the group was performed reflexology interventions within 10 weeks, once a week for 45 min. Data were collected through a structured questionnaire, immediately after.

Results: All expressed satisfaction with the interventions, among them, 7 (58%) reported reflexology benefits in both psychological symptoms and pain, and 5 (42%) in exclusively psychological.

Conclusions: The results showed that, according to the participant´s opinion, reflexology in relieving anxiety, stress, depression and pain was effective. Therefore, this method, as an efficient technique, can be recommended for people with MS. However, sufficient scientific evidence should support its effectiveness and safety.

Disclosure: *Nothing to disclose.*

Keywords: Complementary/alternative therapies in MS

(CAM04)

The Effects of Cbd:THC Tincture Oil Reducing Symptoms and Overall Symptom Management Medication Dosages, in Persons with Multiple Sclerosis

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Background: It is now becoming more common for persons with multiple sclerosis (pwMS) to use cannabis to try to alleviate their MS symptoms. A survey of pwMS published in 2017 found that 47% of respondents considered using cannabis to treat their MS symptoms, 26% used cannabis for their MS symptoms, 20% have spoken with their physician about using cannabis, and 16% currently use cannabis (Cofield et al.). Many reviews (Zhornitsky and Potvin, 2012; Jawahar et al., 2013; Koppel et al., 2014; Whiting et al., 2015) agree cannabis might have a positive effect on pain in MS. In addition to the legal status, limited research evidence remains a barrier to understanding the role cannabis can play in pwMS alleviate symptoms. The amount of scientific research in this area is increasing; however, case reports and anecdotes exceed studies;

thus, data regarding cannabis use to treat pain, spasticity, neuropathy and sleep quality in pwMS remains limited.

Objectives: The purpose of this study is to investigate if medicinal cannabis CBD:THC oil tinctures 1.) improve symptoms and 2.) reduce overall symptom management medication dosages in pwMS. We hypothesize that pwMS will experience improvements in these measures while using CBD:THC tinctures.

Methods: Participants took CBD:THC tincture oil daily. Self-reported symptom and medication assessments rating a scale from 1 to 10 were completed at baseline prior to starting a tincture, and again after an average duration of 3 to 4 months.

Results: 61 pwMS aged 25 and older are included in the study. There were significant reductions ($p < 0.0001$) in the following symptom management scores: pain (from a mean [SD] of 7.4 [2.0] to 3.9 [1.9], n = 45), spasticity (from a mean [SD] of 7.2 [1.9] to 3.3 [1.9], n = 31), neuropathy (from a mean [SD] of 7.7 [2.0] to 4.5 [2.6], n = 25), and sleep (from a mean [SD] of 7.5 [1.9] to 3.0 [2.1], n =34). Gabapentin intake was significantly reduced from a mean [SD] of 1581.3 [1284.6] mg to 625 [739.9] mg (n = 12; p = 0.036). There were no significant reductions in Baclofen, tizanidine, or benzodiazepine intake.

Conclusions: Although medicinal cannabis CBD:THC tincture oil shows promise in overall symptom reduction and symptom management medication dosage reduction in pwMS, researchers need to conduct additional studies, including clinical research studies, for pwMS using medicinal cannabis CBD:THC tincture oil. A larger sample size will allow inferential statistics to be performed. This study will further contribute to the evidence related to the efficacy of this intervention.

Disclosure: *Aryn Sieber: CannaCauses Foundation (consulting fee). Kristine Werner, Karen Carera, Ben Thrower, Jacqueline Rosenthal: Nothing to disclose.*

Keywords: Complementary/alternative therapies in MS

(CAM05)

Challenges and Opportunities in Progressive Multiple Sclerosis Trials: Lessons from Lipoic Acid

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Background: Recruitment for progressive multiple sclerosis (PMS) randomized clinical trials (RCT) is challenging due to 1. Lack of standard definitions of PMS, 2. Varying duration of progression prior to entry, 3. Restricted age and disability requirements, 4. Lack of specific outcome measures with associated sample sizes, 5. Poorly understood PMS natural history, 6. Integration of prior and/or current treatments with disease-modifying therapies (DMT), 7. Integration of emerging DMTs specific for PMS, and 8. Over-the-counter availability of some investigational agents (e.g. lipoic acid, biotin). The resulting narrow inclusion criteria makes recruitment for clinical trials difficult, and raises concerns regarding generalizability of the results.

Objectives: To describe the varying successes of recruitment approaches used in a current multi-site RCT for PMS, compare the resulting study population to other PMS trial populations, and consider if the population is reflective of the general PMS population.

Methods: Describe recruitment methods for Lipoic Acid for Treatment of Progressive MS RCT (LAPMS, NCT03161028). Present the demographic characteristics of the subjects and compare to other PMS study populations and to a general reference PMS population.

Results: LAPMS is a 2 year, multi-site, phase II, double-blind RCT, of LA in PMS (n=118, currently 71% randomized). Enrollment criteria: age $\geq$18 years, non-relapse related MS clinical worsening in prior 2 years, worsening $\geq$ 1 year if on concurrent DMT, EDSS 3.0-6.5, and without non MS-related ambulation deficits. Recruitment sources are: direct from clinic (63.1%), physician referral (23.8%), community outreach/MS events (3.6%), local repository (3.6%), tiny url promotion/NMSS website (2.4%), Facebook advertisement (2.4%), and a NARCOMS recruitment letter (1.2%). Participants have mean age 59.4 (8.1) years, 36 (49.3%) females, median EDSS of 6.0 (3.0-6.5), mean 23.0 (11.7) years since symptom onset, and 9 (12.3%) subjects without previous DMT. Mean LAPMS population age and disease duration is higher than study populations in the EXPAND SPMS trial and ORATORIO PPMS trial. While similar to the EXPAND trial, LAPMS has higher EDSS levels than the ORATORIO population. Updates and comparison to a general PMS population will be presented.

Conclusions: Restrictive PMS recruitment criteria creates differences in PMS trial populations as well as raises concerns about generalizability of results to wider PMS populations. Approaches to addressing these issues are discussed.

Disclosure: *Carin S. Waslo, Mark S. Freedman, Mitchell T. Wallin, Jodie K. Haselkorn: Nothing to disclose. M. Mateo Paz Soldan: Biogen (research funding). Novartis (contracted research). Pavle Repovic: Alexion (consulting fee, speakers bureau). Biogen, EMD Serono (consulting fee, contracted research, speakers bureau). Celgene, Novartis, Sanofi-Genzyme, Viela (consulting fee). Genentech (contracted research, speakers bureau). Genzyme (speakers bureau). Andrew J. Solomon: Actelion, Genentech, Novartis (contracted research). Alexion, Celgene, EMD Serono (consulting fee). Biogen (consulting fee, research funding). John R. Rinker: Biogen-Idec, EMD Serono (contracted research). Rebecca I. Spain: TG Therapeutics (consulting fee).*

Keywords: Clinical Trials, Complementary/alternative therapies in MS, Disease-modifying treatments in MS

(CAM06)

Exercise in Medicine: A Complementary Exercise Promotion Approach within Comprehensive MS Care

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Background: Exercise is one of the only complimentary strategies that improves symptoms of multiple sclerosis (MS), and slows disease progression and functional manifestations. There is further evidence that engaging in exercise regenerates neuroplasticity within the central nervous system. Such evidence supports exercise as a strategy for optimizing independence and quality of live among persons with MS. However, only 20% of the MS population engage in sufficient levels of exercise for accrual of benefits.

Objectives: The objective of this line of work was to develop a new, revolutionary, systematic approach for promoting exercise within comprehensive MS care. This system would reduce the burden of exercise promotion on neurologists whilst allowing patients to receive, timely, accurate information about exercise, and ongoing opportunities and support to engage in this activity

Methods: Over a 6 year period, we conducted interviews with over 80 persons with MS and over 70 health care providers to help design, refine and finalize a new, comprehensive approach to systematically integrate exercise promotion within comprehensive MS care. We also conducted a quality improvement approach to translate the conceptual ideas into a practical context and develop tangible tools to be used to deliver 'Exercise *in* Medicine'.

Results: Through this rigorous line of research, we have built a new, patient-informed, systematic process that integrates exercise promotion within comprehensive MS care; so called 'Exercise *in* Medicine'. Persons with MS and health care providers are supportive of this endeavor and continue to be part of it's refinement and improvement.

Conclusions: 'Exercise *in* Medicine' has the potential to revolutionize the promotion of exercise as a complementary strategy to improve quality of life among persons with MS. This systematic process is now at a stage where it is ready to be tested through clinical trials.

Disclosure: *Nothing to disclose.*

Keywords: Complementary/alternative therapies in MS, Comprehensive care and MS

(CAM07)

Changes in Dietary Habits of Individuals Living with Multiple Sclerosis Enrolled in a Day Wellness Program

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Background:

Nutrition education for individuals who attend the Multiple Sclerosis Achievement Center (MSAC) focuses on overall health and prevention or management of comorbidities. While there has not been a multiple sclerosis (MS)-specific dietary pattern proven to reduce MS symptoms for all individuals, nutritional choices can affect management strategies. Members of the MSAC attend a weekly program that addresses physical, cognitive, and social well-being. On a monthly basis, nutrition education is provided to discuss diverse aspects of dietary habits and target strategies related to the challenges of living with MS. Some program participants receive additional nutrition education through individualized consultations or small group discussions.

Objectives:

To examine the dietary changes of people living with MS who participate in a day wellness program over an 18-month period and determine if changes in habits occur with general nutrition education during the day program. In addition, a comparison in dietary habits between general and individualized nutrition education will be examined.

Methods:

Fifty-two MSAC members have completed Rate Your Plate (RYP), a self-reported food-frequency questionnaire, every six months to monitor changes in dietary choices over a year. RYP consists of 27 questions focusing on typical dietary choices within specified categories. The answer to each question is assigned a score of one, two, or three points with composite scores ranging from 27-81; higher points indicate healthier choices. Between questionnaire administration, members have received monthly nutrition education, with 16 members receiving additional small group nutrition education. Analysis examining 18 month results is planned.

Results:

Three of four intended rounds of data collection have occurred, with the fourth scheduled in February 2020. The mean baseline RYP score was 58.48 (SD= 8.5). The mean of the scores at six-months increased, but not significantly, to 62.33 (SD=7.7; p= 1.00). Increases at one year were statistically significant, 63.71 (SD=7.5; p< .001) compared to baseline. Paired t-tests were used to identify statistical significance. The category showing the greatest improvement (10%) over the first year was the sugar content of desserts. Another improvement (9%) is the frequency in which members are eating meals out.

Conclusions:

Complete collection and analysis of changes between four data collection points will be finalized for presentation of the poster.

Disclosure: *Zoe Edwards, Tiffany Malone: Nothing to disclose. Brian Hutchinson: Biogen (speakers bureau).*

Keywords: Complementary/alternative therapies in MS, Dietary changes

Case Reports / Case Series

(CRS01)

Seasonal Variation and Other Observations in Myelin Oligodendrocyte Glycoprotein (MOG) Antibody-Associated Disease

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Background: MOG antibody-associated disorders can mimic multiple sclerosis (MS). MOG antibody seropositivity has been found in subsets of patients with demyelinating disease, especially those with optic neuritis and transverse myelitis. Improved MOG antibody-associated disease understanding is necessary to improve diagnosis timing and provide proper treatment.

Objectives: To evaluate the characteristics of patients with a confirmed diagnosis of MOG antibody-associated disease.

Methods: We report on the clinical and imaging characteristics of all patients who presented to our practice with optic neuritis or transverse myelitis, and tested positive for MOG antibody between August 2018 and January 2020.

Results: We identified 11 patients, of which 9 (82%) were females. Ten (91%) patients presented between September and December. Optic neuritis preceded by a prodromal headache was the presenting symptom in all patients. Sixteen optic nerves in the 11 patients were symptomatic. Of the 16 symptomatic optic nerves, 12 (75%) nerves showed increased signal on diffusion-weighted imaging (DWI). Incomplete clinical recovery was observed in 11 (69%) optic nerves and ranged from no light perception to a mild decrease in visual acuity. Spinal cord lesions were present in 4 patients (36%). Poorly demarcated white matter brain T2 signal abnormalities were present in 7 patients (64%). Finally, patients younger than 40 years in age tended to have higher titers with 5/6 (83%) patients in this age group having a titer of 1:1000. No patients 40 years and older had a titer of 1:1000. All patients received treatment with prednisone or steroid sparing agents (rituximab or mycophenolate). None of the treated patients relapsed over the duration of the study. One patient was initially misdiagnosed as MS and was treated with several disease modifying agents; he continued to relapse (with sustained disability) until the correct diagnosis was confirmed.

Conclusions: Our findings suggest seasonal variation of MOG antibody-associated disease, with peak clinical presentation during fall and winter months. This may be due to the peak of respiratory viral infections in the fall and winter as preceding infections were reported in association with MOG antibody-associated disease. Increased DWI signal of optic nerves may provide insight into the mechanism of optic nerve damage. Incomplete recovery of optic neuritis is common but often mild and rarely resulted in blindness. The significance of higher antibody titer in younger individuals requires further investigation. Our observations contribute to the growing knowledge of MOG antibody-associated disease, a mimicker of MS. Our study was limited by a small sample size.

Disclosure: *Allison N. Block: Nothing to disclose. Ahmed Z. Obeidat: Alexion (speakers bureau). Alexion Pharmaceutical, Celgene, EMD Serono, Genentech, Sanofi/Genzyme (consulting fee). Biogen, Novartis (consulting fee, speakers bureau). International Journal of MS Care (editorial board).*

Keywords: Imaging and MS, Mimickers of MS, Natural history of MS

(CRS02)

Multiple Surgery and Misdiagnosis before Multiple Sclerosis Diagnosis: A Case Report

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A delay in diagnosis of MS can increase the amount of disability in patients. A 50-year-old Puerto Rican male patient reports onset of symptoms on 1994 with a severe headache that lasted 6 months. A year later patient fell and after started experiencing gait difficulties, pain and bowel and bladder problems. After CT was done, he was diagnosed with herniated discs, and treated with physical, massage and chiropractic therapies. Afterwards, he had frequent falls and facial palsy for 5 years. On these years he had several surgeries performed due to the pain and symptoms. Patient continued with his symptoms after surgeries. Physiatrist evaluated and on 2017 performed brain and cervical MRI and referred to neurologist. Patient was diagnosed with MS on 2018 and assigned an EDSS of 6.0. The time from first symptom to diagnosis (24 years) and the amount of surgeries could have influenced in the disability that the patient presents. This case brings to attention the importance of earlier diagnosis and treatment of MS to reduce disability and improve quality of life in patients. Also, it highlights that we still need to increase education to all health care professionals in Puerto Rico about symptoms, tests and diagnostic criteria for MS.

Background: not applicable

Objectives: not applicable

Methods: not applicable

Results: not applicable

Conclusions: not applicable

Disclosure: *Nothing to disclose.*

Keywords: Comprehensive care and MS, Natural history of MS

(CRS03)

Head Trauma As Onset for MS Diagnosis: A Case Report

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Recent studies found an increased risk of developing MS if head trauma was experienced during teenage years, even though, the relationship of head injury and risk of developing multiple sclerosis (MS) is not clear among the adult population. Previous research in PR MS patients shows that 38.2% reported some type of trauma. We aim to report a case of head injury and

subsequent diagnosis of MS. A 47-year-old Puerto Rican female patient with no previous history of comorbidities. Patient was walking, fell and had head trauma. Concerned, she went to general medicine physician and CT was performed. Months later, patient started presenting pain on R leg, but was diagnosed with urinary tract infection and treated. After this, patient developed episodes of nausea and high levels of leukocytes. On May 2019, developed blurry vision that ended on vision loss on R eye. Ophthalmologist evaluated and referred to neuro-ophthalmologist which ordered MRI. She later developed loss of balance and increased falls and was subsequently diagnosed with Multiple Sclerosis on June 2019. This case highlights the importance of creating awareness among patients that suffered head trauma and present neurological symptoms. Performing tests like magnetic resonance as soon as symptoms start could help to achieve an early diagnosis and help reduce disability among MS patients.

Background: not applicable

Objectives: not applicable

Methods: not applicable

Results: not applicable

Conclusions: not applicable

Disclosure: *Nothing to disclose.*

Keywords: Comprehensive care and MS

(CRS04)

Team Approach Yields Surprising Functional Progress and Quality of Life Changes for a Challenging Person with Nmo

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Background: 59-year-old female (DR) diagnosed with Neuromyelitis Optica (NMO) in February 2016. She developed sudden onset of paralysis and had no voluntary movement from her neck down. DR spent extensive time in a nursing facility and eventually transferred home on a stretcher. At the time of her diagnosis, she was 5'5" tall with BMI 49.08. A rehabilitation team approach from May 2017 through Feb 2020 led to surprising functional progress and improved quality of life.

Objectives: May 2017 DR was referred to a MS Wellness Program. All mobility was dependent to include Hoyer transfers, sitting balance, bed mobility and bowel/bladder management in bed. She also had significant neurological muscle weakness (2-/5 throughout), spasticity, joint contractures and chronic pain from arthritis in her knees, back and shoulders.

Methods: DR attended MS Wellness appointments via stretcher, until she received a power wheelchair. Exercise Specialist (ES) intervention was 2 x week and included pool program, dryland exercises for stretching, strengthening and sitting balance. One year later (May 2018) she began slide board (SB) transfers. By 2019 transfers were via depression and she started using a hydraulic standing device during ES sessions.

October 2019 DR was referred to outpatient Physical Therapy (PT). Her strength was grossly 3-/5, she had contractures at bilateral hips/knees/ankles, and she was unable to stand or walk at home. Her BMI was 43.27. DR attended PT 2-3 x week for 30 sessions to include standing frame and soft tissue work for contractures, transfer training with 3 in 1 bedside commode (BSC), progressive gait training and custom home program.

Results: November 2019, DR achieved supervision for transfers on/off BSC and began gait training in parallel bars (PBars) with bilateral malleoloc braces and heel wedges. Sit/stand and stepping in PBars progressed from Max A to Supervision. By mid December 2019 she required Mod A to walk outside the PBars with front wheeled bariatric walker (FWBW). End of December 2019 she required Min A to walk up to 76 ft for exercise. In early February 2020 patient was able to walk 135 ft at a time with close stand by assist (SBA) with FWBW and bilateral solid Ankle Foot Orthoses (Bil AFOs). She walked over indoor and outdoor terrains including 5 degree ramps. After caregiver training, she became safe to stand and walk at home for exercise.

Conclusions: After being completely paralyzed after NMO diagnoses in 2016, DR spent nearly 3 years attending a MS Wellness Program and then eventually outpatient PT. She progressed from being totally dependent to requiring supervision for all transfers. She no longer had to use bed pans. Additionally, she learned to walk with SBA indoor/outdoor terrains with FWBW and bilateral AFOs. DR's functional gains and improved quality of life would have been very unlikely without a team approach. DR is to be commended for her determination and as health care professionals we should always keep an open mind.

Disclosure: *Nothing to disclose.*

Keywords: Complementary/alternative therapies in MS, Comprehensive care and MS, Wellness Program

(CRS05)

Differential Diagnosis and Treatment of Tumefactive Demyelination in a Teenaged Girl

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Background: Tumefactive demyelination in pediatric patients is rare and associated with high morbidity and mortality. The differential diagnosis includes tumor, abscess, acute hemorrhagic leukoencephalitis (AHLE), acute disseminated encephalomyelitis (ADEM) and tumefactive MS. Awareness of the differential and early treatment is essential as this presentation may be associated with death or severe morbidity within days.

Objectives: Review a case of tumefactive demyelination in a teenaged girl, and review the pertinent literature, including differential diagnosis, key clinical characteristics, and treatment options

Methods: Medical record review and review of the literature.

Results: A 16 year old girl, previously healthy and developmentally normal, presented with encephalopathy progressing quickly to left hemiparesis and global aphasia in the setting of recent upper respiratory infection with cough, headache, and otalgia. Head CT demonstrated vasogenic edema of the left temporal and parietal lobes and 4mm of midline shift to the right, without obvious underlying mass. MRI of the brain revealed extensive confluent and expansile-appearing white matter signal abnormality of the left brainstem, internal capsule, parietal and temporal lobes with associated microhemorrhages and left cerebral peduncle and pontine enhancement, suggestive of severe demyelinating disease, and her CSF showed a neutrophilic pleocytosis with no identifiable pathogen. A brain biopsy showed no signs of neoplasm. She was promptly treated with high dose prednisolone, and the course continued for 7 days in conjunction with 9 rounds of plasmapheresis. Cyclophosphamide was initiated with a plan for a 6 month course. Follow-up MRI of the brain one month after presentation demonstrated decreased extent of T2/FLAIR abnormality and development of cystic encephalomalacia along the left anterior temporal lobe with resolution of midline shift. She was transferred to the inpatient rehabilitation service for a one month stay. At discharge she had persistent right sided weakness with spasticity but was able to ambulate using a single crutch, and had shown improvement in expressive and receptive aphasia.

Conclusions: Tumefactive demyelination requires rapid evaluation and treatment. The differential diagnosis includes AHLE, which has a particularly high fatality rate. Early and judicious immunomodulatory treatment in these cases is lifesaving

Disclosure: *Nothing to disclose.*

Keywords: Disease-modifying treatments in MS, Imaging and MS, Immunology and MS

(CRS06)

A Long Standing Case of Recurrent Transverse Myelitis Due to Mog-IgG Antibody Mimicking Multiple Sclerosis

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Background:

Myelin Oligodendrocyte Glycoprotein (MOG) IgG antibody causes central nervous system demyelination and mimics Multiple Sclerosis (MS). Patients with MOG-IgG typically present with recurrent or monophasic optic neuritis, transverse myelitis, conus medullaris lesion, brainstem encephalitis, steroid dependent symptoms and acute disseminated encephalomyelitis. Lack of testing for MOG-IgG in these patients can lead to an incorrect diagnosis of MS and treatment with certain medications that can worsen MOG-IgG associated disease.

Objectives: To report a case of a patient with MOG-IgG antibody mediated recurrent transverse myelitis who was diagnosed with possible MS for more than 15 years.

Methods: A 66-year-old woman with a known diagnosis of possible MS presented to our clinic for follow up. Her history dated back to 1989 when she had an episode of extreme fatigue, gait imbalance, and numbness in her hands and feet that resolved spontaneously. She had recurrent episodes of symptomatic myelitis in 1997 and 2001. On examination, she had spastic weakness of bilateral iliopsoas and finger extensors (left worse than right), brisk reflexes on the left hemibody with left ankle clonus, relative sensory level at T12 and spastic ataxic gait without assistance. Timed 25 feet walk was 6.86 seconds.

Results:

In 2001, MRI of the spinal cord showed several short segment lesions in the cervical and thoracic spinal cord including the conus medullaris, MRI of the brain was normal. Cerebrospinal fluid (CSF) showed elevated protein, IgG synthesis rate and CSF specific oligoclonal bands, Aquaporin 4 antibody (AQP-4) in CSF was negative. She was diagnosed with possible MS given the lack of better explanation and was started on a combination of interferon beta-1a and mycophenolate. Since 2001, she did not have clinical relapse though had new nonspecific lesions in her brain and persistently enhancing short segment lesions in the cervical and thoracic spinal cord in 2014 and 2016. Interferon beta-1a was stopped in 2017 and mycophenolate was continued. Serum MOG-IgG was tested and was positive in February 2019.

Conclusions:

MOG-IgG mediated disease and MS show a relevant phenotypic, clinical and radiological overlap that can potentially lead to misdiagnosis and worse patient outcomes as some medications used for the treatment of MS might be ineffective or even harmful in MOG-IgG associated disease. Before the diagnosis of MS, testing for MOG-IgG antibody should be considered in selected patients.

Disclosure: *Nothing to disclose.*

Keywords: Comprehensive care and MS, MOG IgG antibody

(CRS07)

Case Report of Severe Multiple Sclerosis Relapse Due to B Cell Reconstitution Post Alemtuzumab

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Background: Alemtuzumab is a pan-lymphocyte depleting anti-CD52 antibody used in the treatment of Multiple Sclerosis. However, there have been reports of severely exacerbated CNS inflammation following alemtuzumab infusion. Relapse often occurs with the repletion of B cells months after treatment, whereas T cells can take up to 3 years to replenish. B cell reconstitution occurs when the memory B cells replenish more rapidly than the T regulatory cells. This has previously been seen with the use of rituximab as a B cell depleting therapy in disorders such as Rheumatoid Arthritis.

Objectives: Here, we present a case of a 52 year old white female diagnosed with Multiple Sclerosis in 2000. She had previously tried multiple Disease Modifying Therapies including interferon beta 1a, interferon beta 1b, glatiramer, natalizumab, and dimethyl fumarate. She was given round one of alemtuzumab in December of 2018. In May of 2019 she experienced an exacerbation that caused hospitalization for IV methylprednisolone and physical therapy. She made a full recovery to baseline. In July 2019 she experienced another exacerbation, presenting to the clinic with multiple new symptoms including ataxia, urinary incontinence, weakness and numbness. She was treated with repository corticotropin injection with no improvement. This was immediately followed by another hospitalization for plasma exchange. Her symptoms continued to progress rapidly. Brain MRI showed development of innumerable enhancing lesions throughout the bilateral cerebral hemispheres and right lateral pons. Cervical spine MRI showed a new 5mm enhancing lesion. MRI of Thoracic spine showed several enhancing thoracic cord lesions consistent with active demyelinating disease. Due to her rapid deterioration, the decision was made to transfer her to another state to receive a higher level of care. After being evaluated it was determined that she likely had active demyelination related to B Cell Reconstitution. She

was again hospitalized and received one dose of rituximab. Unfortunately, as of October 2019, the patient has continued to decline.

Methods: N/A

Results: She was discharged home on hospice and passed away a week later. An autopsy was performed and the results are pending at this time.

Conclusions: This case signifies the importance of strict monitoring of B Cells post alemtuzumab due to the risk of relapse as the B cell population returns. Further analysis is needed for optimal care of these patients.

Disclosure: *Jennifer Chester: Allergan, Biogen, Novartis, SanofiGenzyme (speakers bureau). Tyler Kaplan: Nothing to disclose.*

Keywords: Disease-modifying treatments in MS, Immunology and MS, Nursing management in MS

(CRS08)

Demographics, Clinical Characteristics, and Outcomes of Mog Antibody Disease Followed at Washington University in St. Louis

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Background: Antibodies to myelin oligodendrocyte glycoprotein (MOG) have been associated with CNS demyelination that is distinct from other neuroinflammatory conditions. Our knowledge of the clinical spectrum of MOG antibody disease (MOGAD) is evolving, without clear understanding of prognosis and best treatments.

Objectives: To report demographics, clinical characteristics, and treatment responses of our MOGAD cohort.

Methods: Patients at Washington University were identified via diagnosis code and confirmed to have at least one positive MOG antibody test. Demographic, clinical course, estimated disability (extracted using published tools), laboratory, and treatment data were collected after IRB approval.

Results: 24 MOGAD patients were included. They were 75% female and 92% Caucasian with mean onset age of 43.5 years (range 16.8-76.0 years). Average duration of follow-up was 4.0 years (range 0.4-18.0 years). Initial symptoms exclusively included optic neuritis (17/24, 41% bilateral) or transverse myelitis (9/24), with 2/24 having both occur simultaneously. 12.5% (3/24) had concurrent involvement of other areas (brainstem, cerebral). A total of 42 attacks

(including initial onset) were adjudicated; the annualized relapse rate was 0.46. 42% have had only a single attack. Attacks tended to be severe (estimated ΔEDSS +3.3), followed by complete recovery in 35% and no recovery in 21%. Most (81%) attacks were treated with corticosteroids. 38% of all patients have remained stable without chronic treatment, but 79% of those with relapses were on no chronic treatment. Rituximab was associated with a low relapse rate, though breakthrough relapses still occurred in 2 patients. 4 patients had 3+ attacks: all had optic neuritis, and 3 were exquisitely sensitive to decreases in their maintenance corticosteroid dose. 54% of patients had multiple MOG antibody titers (average 7.2 months later), of whom 31% became seronegative. None of these patients relapsed after testing negative. CSF testing was modestly abnormal (median cell count 8, average protein 56.9). No patients had >2 CSF-specific oligoclonal bands. In those with 2+ years of follow-up, 50% remained relapse-free. In those with 5+ years of follow-up, 44% remained relapse-free. Average current EDSS is 1.9. 58% have an EDSS ≥2.0, and 13% have an EDSS ≥4.0.

Conclusions: We report a cohort of Midwestern patients with anti-MOG disease. Our results are largely consistent with those reported in other cohorts of this disease.

Disclosure: *John R. Ciotti: Nothing to disclose. Anne Cross: Biogen, Celgene, Novartis, TG Therapeutics (consulting fee). EMD Serono, Genentech/Roche (grant and personal fees). Salim Chahin: Biogen, Genentech, Novartis, Sanofi Genzyme, Teva Neuroscience (personal fees).*

Keywords: MOG antibody disease

(CRS09)

A Fatal Case of Alemtuzumab Induced Immune Thrombocytopenic Purpura in a Patient with Relapsing Multiple Sclerosis

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Background: Alemtuzumab is a humanized monoclonal antibody against CD52 approved for relapsing types of multiple sclerosis. Despite being an effective medication, there have been limitations of use for this medication due to various serious side effects. Common side effects include infections, transfusion reactions and, autoimmune responses such as hemolytic anemia, thrombocytopenia and autoimmune thyroid and renal disease.

Objectives: To review a case of refractory immune thrombocytopenic purpura (ITP) as a result of Alemtuzumab therapy who presented with altered mental status and found to have multiple foci of intracranial bleeding (ICH).

Methods: Case Report

Results: Our patient was a 39-year-old female who developed ITP after receiving two doses of alemtuzumab. The patient passed two years after the initial Alemtuzumab infusion after dealing with multiple comorbidities due to refractory ITP. According to the literature, ITP occurs to 2-2.6% of patients treated with alemtuzumab. ITP can be refractory and fatal; however, in CAMMS223 study only 1 out of 6 patients with ITP died due to ICH. In addition, in two other studies on MS patients receiving Alemtuzumab, no ITP associated mortality is reported.

Conclusions: Alemtuzumab is a potent immune regulator that clears up T-cells and B-cells. ITP is a rare complication but can be lethal. Our patient's ITP progressed despite her compliance with q6 month blood count checks and receiving various treatments. The aim of this presentation is to bring the potentially serious complications of alemtuzumab to attention and consider substitute therapies if feasible.

Disclosure: *Nothing to disclose.*

Keywords: Comprehensive care and MS, Disease-modifying treatments in MS, Immunology and MS

(CRS10)

Colitis Associated with Teriflunomide

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Background:

Teriflunomide is an oral disease modifying therapy for relapsing remitting multiple sclerosis (RRMS) which was approved in the US in 2012.

Gastrointestinal (GI) side effects occurred in 15-17% of patients in the clinical trials and so far, three cases of colitis have been reported.

Objectives:

To report new onset Crohn's disease in an MS patient while on teriflunomide.

Methods:

Case report and literature review

Results:

A 49 year-old man with RRMS started teriflunomide in 1/2018 after discontinuing glatiramer acetate due to injection fatigue and dimethyl fumarate due to GI intolerability. He developed persistent diarrhea in 7/2018; GI work up showed non-bleeding gastric ulcers and mild chronic gastritis without active inflammation in the small and large intestine. GI disease improved with omeprazole and stopping ibuprofen; teriflunomide was reduced to 7 mg daily in 12/2018.

In 8/2019, he experienced recurrence of significant diarrhea and weight loss. Teriflunomide was stopped and he was started on colestipol with notable improvement in his diarrhea. Repeat endoscopy showed multiple duodenal ulcers, gastric ulcers, esophagitis and ulcerations throughout the colon and terminal ileum. Pathology demonstrated inflammatory changes consistent with inflammatory bowel disease. He was started on vedolizumab for Crohn's disease in 11/2019.

Conclusions:

In 2017, Health Canada released a review on teriflunomide due to post marketing reports of colitis and concluded that while no definite link could be established, the patients and providers should be alerted to the occurrence of rare colitis cases.

As of October 2019, per Genzyme three cases of colitis while on teriflunomide are reported of which two were considered to be related to teriflunomide. We here report a case of new onset of inflammatory colitis with endoscopic and pathological features of Crohn's disease while on teriflunomide and significant improvement after cessation of the drug and suggest potential causal relationship between the drug and development of colitis which warrants further investigation.

Rare cases of colitis have occurred in patients on teriflunomide including a recent case of new onset of Crohn's disease. While the association remains unclear, physicians should be aware of this potential side effect. Clinical vigilance and early treatment might be helpful in cessation of colitis progression.

Disclosure: *Neda Zarghami Esfahani, Gloria von Geldern, Meghan C. Romba, Dhavan Parikh: Nothing to disclose. Annette Wundes: Biogen (consulting fee). Biogen, Abbvie (contracted research).*

Keywords: colitis, Disease-modifying treatments in MS

(CRS11)

Remarkable Recovery of Fulminant Multiple Sclerosis after Treatment Induction with Cyclophosphamide

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Background: Fulminant multiple sclerosis (MS) is rare and the approach to treatment beyond first line therapies (high dose steroids, plasma exchange, and intravenous immunoglobulins) varies. Single case reports of diagnosis and treatment of fulminant MS can provide helpful resources for the clinician. Cyclophosphamide is a alkylating agent that suppresses T and B cell function, interleukin 12, and T-helper type 1 (Th1) responses thereby enhances Th2, Th3 responses. Review of published reports suggests that Cyclophosphamide has utility in early stages of MS during which inflammation predominates over degenerative processes in the central nervous system as seen by gadolinium (Gd)-enhancing lesions.

Objectives: To describe the clinical course of a case of acute MS successfully treated with cyclophosphamide.

Methods: Case study.

Results: A 41 year old woman with no medical history developed facial paresthesia, imbalance and dizziness. Neurological examination showed hyperreflexia. MRI showed numerous Gd-enhancing white matter lesions throughout the brain, cervical and thoracic spinal cord. Initial treatment with 1000 mg of IV methylprednisolone did not result in symptom improvement but decreased the burden of enhancing lesions on repeat MRI. On hospital day 8, she clinically deteriorated, and plasma exchange was initiated. She continued to worsen and developed respiratory failure requiring mechanical ventilation, cranial nerve palsies and quadriplegia. IVIG was given with no clinical response. A brain biopsy obtained due to concern for lymphoma but it showed severe demyelination with relative axonal preservation. Due to significant clinical deterioration, we proceeded with induction treatment with cyclophosphamide (600mg/m2 daily for 4 doses). Treatment resulted in gradual clinical and radiological improvement. For maintenance therapy, she received one dose of IV rituximab 1000 mg and was discharged to a long-term acute care facility. Subsequently she was weaned off mechanical ventilation, significantly restored upper limb functions and is able to walk for more than 40 feet with assistance. At day 104 from initial presentation, she continues to improve with no new relapse activity. Follow up MRI brain and spinal cord 21 days after discharge demonstrated resolution of most of the lesions, interval improvement of some and no new or enhancing lesions identified.

Conclusions: Induction therapy with cyclophosphamide combined with supportive care can help improve acute fulminant demyelination.

Disclosure: *Nicola Carlisle, Sam I. Hooshmand, Michelle Maynard: Nothing to disclose. Ahmed Z. Obeidat: alexion, biogen (consulting fee, speakers bureau). celgene, EMD serono, genen tech, sanofi (consulting fee). International journal of MS (editorial board). Novartis (speakers bureau).*

Keywords: Disease-modifying treatments in MS, Imaging and MS

(CRS12)

Neurofibromatosis 1 and Multiple Sclerosis in the Same Patient

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Background: Neurofibromatosis type 1 (NF1) is an autosomal-dominant genetic disease involving primarily the skin and peripheral nervous system. Multiple sclerosis (MS) is a demyelinating disease of the central nervous system. White matter lesions on MRI brain can be seen in both diseases. Only few cases have been reported to-date describing patients with both MS and NF1.

Objectives: To describe three cases of comorbid NF1 and MS in order to raise awareness of the possibility for the rare co-occurrence of both conditions.

Methods: This is a detailed description of three cases and a literature review of co-occurring NF1 and MS. Electronic medical records, neuroimaging, and relevant ancillary tests were reviewed for all cases.

Results: A 21-year-old man with NF1 presented with an episode of several days of bilateral distal limb paresthesias and was found to have brain and spine lesions, some of which were enhancing. Optic nerves with likely optic glioma due to NF1 as well as possible prior optic neuritis. Cerebrospinal fluid (CSF) showed positive oligoclonal bands. He was started on glatiramer as disease modifying therapy, which was advanced to natalizumab based on significant radiographic disease progression. The second case is a 41-year-old woman with NF1 who presented with optic neuritis (with improvement with high dose steroids) and was found to have lesions on MRI brain and spine and positive oligoclonal bands in CSF. She was started on glatiramer acetate with clinical stability and only one new non-enhancing lesion on repeat MRI. Due to skin reactions on glatiramer acetate, she was changed to dimethyl fumarate. A 40-year-old female with NF1 presented with progressive gait changes. Based on MRI findings more suggestive of MS than NF1 and positive oligoclonal bands in CSF she was diagnosed with primary progressive multiple sclerosis.

Conclusions: These cases demonstrate the rare co-occurrence of NF1 and MS as well as the heterogeneity of MS presentations within the NF1 patient population. These cases also demonstrate some of the diagnostic challenges that arise when making a new diagnosis of MS in patients with NF1, including the interpretation of MRI in differentiating suspected demyelinating

lesions from lesions that are associated with NF1. It is unclear if the co-occurrence of NF1 and MS is coincidental or if these cases represent an unknown relation between the two diseases.

Disclosure: *Annette Wundes: AbbVie, Alkermes (contracted research). Biogen (consulting fee, contracted research). Sargon Bet-Shlimon, Gloria von Geldern: Nothing to disclose.*

Keywords: Diagnosis and management of MS, Epidemiology of MS, Imaging and MS

(CRS13)

Successful Use of Immunotherapy for Osmotic Demyelination Syndrome

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Background:
Osmotic demyelination syndrome (ODS) is a disorder characterized by the destruction of neuronal myelin sheaths in the pons or other susceptible areas, usually due to the rapid correction of hyponatremia, often with irreversible neurological consequences. The standard of care is supportive treatment.

Objectives: To highlight the novel use of immunotherapeutic strategies in patients with ODS

Methods: Case Report

Results:
This is a case of a 44 year old male with chronic alcohol abuse and hyponatremia due to beer potomania who presented with acute encephalopathy and rapidly progressive quadriplegia. Initial sodium level was 102 mm/L. Due to septic shock and concern for rhabdomyolysis, he was aggressively fluid resuscitated. Sodium levels increased by 3 points every 2 hours, ultimately normalizing within 24 hours. MRI brain showed areas of abnormal FLAIR signal hyperintensity within the pons and bilateral basal ganglia without enhancement. He was given 5 treatments of plasmapheresis followed by 5 days of intravenous immunoglobulin. 10 months later, he was ambulatory and independent in his activities of daily living. His only deficit was weakness in left wrist extension and flexion with contractures in the 4th/5th digit.

Conclusions:
Immunotherapy such as plasmapheresis, intravenous immunoglobulin, or a combination may provide a treatment approach for patients with ODS where options are extremely limited. Timing from symptom onset to treatment initiation is crucial, ideally within a week. Recovery can be slow. Patient selection may also inform outcomes as benefit seems to be in those with chronic alcohol abuse or hepatic dysfunction.

Disclosure: *Nothing to disclose.*

Keywords: Complementary/alternative therapies in MS

Disease-modifying Therapy

(DXT01)

Maintenance of Working Status and Work Productivity in Persons with Multiple Sclerosis Treated with Dimethyl Fumarate: A 5-Year Analysis of the Narcoms Registry

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Background: Employment is often affected in persons with multiple sclerosis (MS), and changes in employment status are associated with reduced quality of life. However, there is limited research on the maintenance of employment and work productivity in persons with MS using a disease-modifying therapy.

Objectives: To evaluate working status and work productivity in persons with relapsing remitting multiple sclerosis (RRMS) treated with dimethyl fumarate (DMF) for up to 5 years.

Methods: In this analysis, we included RRMS registry participants from the US who reported DMF initiation in any semi-annual update survey between Fall 2013 and Spring 2018; participants also had to have ≥1 year of follow-up data. The index survey was considered the survey when DMF was initiated. Work productivity was assessed by reported reduction in hours worked (yes/no) and number of work days missed. Time to change in working status (employed full-time to part-time, employed full- or part-time to not working) was evaluated using the Kaplan-Meier method. Participants were censored at last follow-up or DMF discontinuation, whichever came first.

Results: A total of 608 RRMS participants initiated DMF within the study period and had follow-up at 1 year. There were 294 (48.4%) participants employed at initiation of DMF (full-time, 73.8%). Most employed participants were female (86.1%), Caucasian (82.6%), had a bachelor's degree or higher education level (65.1%), and the mean (SD) age was 47.7 (9.5) years. The mean (SD) age at diagnosis was 36.0 (8.3) years. The median (interquartile range [IQR]) PDDS level at initiation was 1 (0, 7) and median (IQR) follow-up was 2 (1, 3.5) years. Overall, 49 (16.7%) participants decreased employment; 13 (4%) changed from full-time to part-time status, and 36 (12%) changed from employed (full- or part-time) to not working. During follow-up, 31 (10.5%) reported reducing their hours worked and there was a median of 3 (1, 6)

missed work days per year. Of the 314 participants not employed, 23 (7.3%) participants went from not employed to employed.

Conclusions: Among NARCOMS participants who were treated with DMF for up to 5 years, most maintained their baseline level of working status and maintained stable levels of work productivity as assessed by missed work days and the proportion reducing work hours. The NARCOMS registry provides an opportunity to longitudinally assess outcomes in DMF-treated persons with MS.

Support: Biogen. NARCOMS is a project of the CMSC.

Disclosure: *Amber Salter: Circulation: Cardiovascular Imaging (circulation: cardiovascular imaging). Samantha Lancia: Nothing to disclose. Gary Cutter: AMO Pharmaceuticals, Biolinerx, Brainstorm Cell Therapeutics, Galmed Pharmaceuticals, Hisun Pharmaceuticals, Horizon Pharmaceuticals, Merck, Merck/Pfizer, Neurim, NHLBI (Protocol Review Committee), NICHD (OPRU oversight committee), Ophazyme, Opko Biologics, Reata Pharmaceuticals, Receptos/Celgene, Sanofi-Aventis, Teva Pharmaceuticals (data and safety monitoring committees). Biogen, Click Therapeutics, Genentech, Genzyme, GW Pharmaceuticals, Klein-Buendel Incorporated, Medday, Medimmune, Osmotica Pharmaceuticals, Perception Neurosciences, Recursion Pharmaceuticals, Roche, Somahlution, TG Therapeutics (consulting fee). Novartis (consulting fee, data and safety monitoring committees). Robert J. Fox: Actelion, Biogen, Immunic, Novartis (advisory committee, consulting fee). Celgene, EMD Serono, Genentech, Teva (consulting fee). Ruth Ann Marrie: Multiple Sclerosis Journal-ETC (multiple sclerosis journal-etc). Jason P. Mendoza, James B. Lewin: Biogen (ownership interest, salary).*

Keywords: Dimethyl fumarate, Disease-modifying treatments in MS

(DXT02)

Early Effect of Ofatumumab on B-Cell Counts and MRI Activity in Relapsing Multiple Sclerosis Patients: Results from the Aplios Study

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Background:

B cells play a major role in the pathogenesis of multiple sclerosis (MS). Ofatumumab, the first fully human anti-CD20 monoclonal antibody, with a monthly 20 mg subcutaneous (s.c) dosing regimen suppressed 94–98% of the gadolinium-enhancing (Gd+) lesions versus teriflunomide in the Phase 3 ASCLEPIOS I/II relapsing multiple sclerosis (RMS) trials. In APLIOS, the onset of ofatumumab effect on B-cell depletion and MRI activity can be determined.

Objectives:

To evaluate the onset of ofatumumab 20 mg s.c. effect on B-cell depletion and suppression of Magnetic Resonance Imaging activity in RMS patients.

Methods:

APLIOS was a 12-week, open-label, Phase 2, bioequivalence study in RMS patients (N=284) who received ofatumumab 20 mg (0.4 mL) s.c. loading doses on Days 1, 7, and 14, and maintenance doses every 4 weeks from Week 4 via an autoinjector pen (SensoReady) or a prefilled syringe. Suppression of CD19+ B cells was measured 9 times over 12 weeks. Gd+ lesion counts were assessed at baseline and at Weeks 4, 8, and 12.

Results:

Ofatumumab rapidly depleted circulating B cells, from a median B-cell count of 219 cells/µL (Day 1) to 10 cells/µL (Day 4) and 1 cell/µL by the end of the loading regimen (Week 4). The proportion of patients with B-cell counts of <10 cells/µL was >65% after the first injection by Day 7, 94% by Week 4, and sustained >95% at all following injections. Ofatumumab treatment reduced the mean number of Gd+ lesions from 1.5 (baseline) to 0.8, 0.3, and 0.1 by Weeks 4, 8, and 12, respectively; the proportion of patients free from Gd+ lesions at the corresponding time points were 66.5%, 86.7%, and 94.1%.

Conclusions:

Ofatumumab 20 mg s.c. monthly dosing regimen resulted in a rapid, close-to-complete and sustained B-cell depletion over 12 weeks, leading to a profound reduction of Gd+ lesions in RMS patients, consistent with the effects observed in the pooled Phase 3 ASCLEPIOS I/II patient population.

Disclosure: *Amit Bar-Or: Atara Biotherapeutics, Biogen Idec, Celgene/Receptos, Genentech/Roche, GlaxoSmithKline, MAPI, MedImmune, Merck/EMD Serono, Novartis, Sanofi Genzyme (consulting fee, speakers bureau). Edward J. Fox: Biogen, Celgene, Chugai, EMD Serono, Genentech/Roche, MedDay, Novartis, Sanofi, Teva, TG Therapeutics (advisory work, consulting fee, contracted research, speakers bureau). Genzyme (advisory board, contracted research, speakers bureau). Alexandra Goodyear, Inga Ludwig, Morten Bagger, Dieter A. Haering, Harald Kropshofer, Martin Merschhemke: Novartis (salary). Heinz Wiendl: Bayer HealthCare, Biogen, Fresenius Medical Care, GlaxoSmithKline (consulting fee, honoraria).*

Keywords: Disease-modifying treatments in MS, Imaging and MS, Immunology and MS

(DXT03)

Analyses of the Effect of Disease Duration on the Efficacy and Safety of Siponimod in Patients with Active SPMS from the Expand Study

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Background: Siponimod (Mayzent®) is a selective sphingosine 1-phosphate receptor ($S1P_1$ and $S1P_5$) modulator, approved in the USA for treatment of relapsing forms of multiple sclerosis (MS), including clinically isolated syndrome, relapsing-remitting MS and active secondary progressive MS (SPMS). In the phase 3 EXPAND registration trial in SPMS, siponimod significantly reduced risk of 3 (primary endpoint) and 6 month confirmed disability progression (CDP) by 21% and 26%, respectively.

Objectives: Assess efficacy and safety of siponimod in patients with active SPMS in subgroups of patients with MS duration (time since onset of first symptoms) of <16 or ≥16 years ([y] median value) at baseline.

Methods: *Post hoc* analyses were performed in patients with active SPMS, defined as a relapse in the 2 y before screening and/or ≥1 T1 Gd+ lesion at baseline, randomized to siponimod 2 mg qd or placebo. Efficacy endpoints: time to 3 and 6 month CDP (as per Expanded Disability Status Scale scores). Adverse events (AEs), serious AEs, and AEs leading to treatment discontinuation were assessed. Analyses for hypothesis generation, without adjustment for multiple comparisons.

Results: There were 779 patients with active SPMS: 427 with MS duration <16 y (siponimod n=285; placebo, n=142) and 352 with ≥16 y duration (siponimod n=231; placebo, n=121). For MS duration of <16 y, siponimod reduced 3 and 6 month CDP risk by 32.4% and 42.7%, respectively, versus placebo (3 month: siponimod, n=68 [23.9%]; placebo, n=48 [33.8%]; hazard ratio [HR], [95% confidence interval (CI)]: 0.68, [0.47, 0.98]; p=0.0378; 6 month: siponimod, n=48 [16.8%]; placebo, n=40 [28.2%]; HR, [95% CI]: 0.57, [0.38, 0.87]; p=0.0093). For MS duration ≥16 y, siponimod had a trend towards reduced 3 and 6 month CDP risk of 31.9% and 27.1%, respectively, versus placebo (3 month: siponimod, n=61 [26.4%]; placebo, n=43 [35.5%]; HR, [95% CI]: 0.68, [0.46, 1.01]; p=0.0540; 6 month, siponimod, n=51 [22.1%]; placebo, n=34 [28.1%]; HR, [95% CI]: 0.73, [0.47, 1.13]; p=0.1544). Siponimod was generally well tolerated. Any AE rates were: <16 y, 84.9% (siponimod), 75.4% (placebo); ≥16 y, 89.2% (siponimod), 81.8% (placebo).

Conclusions: In patients with active SPMS and MS duration <16 years, siponimod significantly reduced 3 and 6 month CDP risk compared with placebo. Siponimod showed a trend towards reduced CDP versus placebo in those with duration ≥16 years. This may reflect the smaller size or more advanced disease in this subgroup.

Disclosure: *Amit Bar-Or: Atara Biotherapeutics, Bayer, Bayhill Therapeutics, Berlex, Biogen Idec, BioMS, Celgene/Receptos, Diogenix, Eli Lilly, F Hoffman-La Roche, Genentech, GlaxoSmithKline, Guthy-Jackson/GGF, Immunic, Janssen/Actelion, MAPI, Medimmune, Merck/EMD Serono, Novartis, Ono Pharmacia, Roche/Genentech, Sanofi-Genzyme, Teva Neuroscience, Wyeth (consulting fee). Stanley L. Cohan: AbbVie, Adamas, Alexion, MedDay, Sage Bionetworks (contracted research). Biogen, Novartis, Sanofi Genzyme (consulting fee, contracted research, speakers bureau). EMD Serono, Pear Therapeutics (consulting fee). Genentech, Roche (contracted research, speakers bureau). Patricia K. Coyle: Accordant, Alexion, Bayer, Biogen Idec, Celgene, Genentech/Roche, Genzyme/Sanofi, GlaxoSmithKline, Mylan, Novartis, Serono, TG Therapeutics (consulting fee). Actelion, Alkermes, Corrona LLD, MedDay, PCORI (research grant). Fred D. Lublin: AbbVie, Acorda Therapeutics, Apitope, Atara Biotherapeutics, Bayer HealthCare Pharmaceutcials, Biogen Idec, Brainstorm Cell Therapeutics, EMD Serono, Foward Pharma, Innate Immunotherapeutics, Mapi Pharma, MedDay Pharma, MedImmune, Novartis, Orion Biotechnology, Polpharma, Recptos/Celgene, Regeneron, Roche Genentech, Sanofi Genzyme, Teva Neuroscience, TG Therapeutics (consulting fee). Actelion (consulting fee, research support). Multiple Sclerosis and Related Disorders (journal) (serving as an editor). NMSS, Novartis Pharmaceuticals, Sanofi, Teva Neurosciences, Transparency Life Sciences (research support). Xiangyi Meng, Wendy Su: Novartis Pharmaceuticals Corporation (salary). Bruce A C Cree: Akili, Alexion, Atara, Biogen, EMD Serono, Novartis, TG Therapeutics (consulting fee).*

Keywords: Disease-modifying treatments in MS

(DXT04)

Siponimod First-Dose Effects in Patients with SPMS Receiving Concomitant Selective Serotonin Reuptake Inhibitor Therapy

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Background: Selective serotonin reuptake inhibitors (SSRIs), citalopram and escitalopram, are associated with prolonged QTc and torsades de pointes; transient heart rate decrease at initiation is a known effect of S1P modulators. Siponimod is a sphingosine 1-phosphate (S1P) receptor type 1,5 modulator, and is metabolized mainly by CYP2C9, followed by CYP3A4. It is approved in the USA for relapsing forms of multiple sclerosis (MS), including CIS, RRMS and active SPMS. First-dose observation with siponimod is only required in certain cardiac conditions but it is important to understand the cardiac effects in patients receiving concomitant SSRIs.

Objectives: Evaluate first-dose effects of siponimod in patients receiving concomitant SSRIs during the EXPAND trial.

Methods: Analyses included data for the overall siponimod group (with or without SSRI), and subgroups of concomitant siponimod and any SSRI at first dose (Day 1), and concomitant siponimod and citalopram or escitalopram on Day 1.

Results: In all, 1105 patients were randomized to siponimod; 167 received an SSRI on Day 1 and 85 received citalopram or escitalopram. For those with extended monitoring, in the overall siponimod group, and the any SSRI and citalopram/escitalopram subgroups, most were discharged at 6 h post first dose (91.1%, 91.4% and 89.6%, respectively). Day 1 after first dose, 4 patients (0.4%) in the overall siponimod group had serious AEs (SAEs), 2 (0.2%) had bradycardia and 1 (0.1%) had second-degree atrioventricular (AV) block; no SAEs occurred in the any SSRI or citalopram/escitalopram subgroups. Few patients in the overall siponimod group had cardiac AEs on Day 1: 29 patients (2.6%) had bradycardia, 4 (0.4%) had first-degree AV block, 3 (0.3%) had second-degree AV block and 3 (0.3%) had prolonged QT interval. Incidence of cardiac AEs was low in the any SSRI subgroup: 3 patients (1.8%) had bradycardia and 3 (1.8%) had prolonged QT interval; in the citalopram/escitalopram subgroup, 2 patients (2.4%) had bradycardia and 1 (1.2%) had prolonged QT interval. In the overall siponimod group, 3 patients (0.3%) discontinued drug due to first- or second-degree AV block, or bradycardia. No patient receiving SSRIs had a cardiac AE causing treatment discontinuation.

Conclusions: Concomitant SSRI use did not appear to affect cardiac outcomes or heart rate changes associated with siponimod treatment initiation.

Disclosure: *Amit Bar-Or: Atara Biotherapeutics, Bayer, Bayhill Therapeutics, Berlex, Biogen Idec, BioMS, Celgene/Receptos, Diogenix, Eli Lilly, F Hoffman-La Roche, Genentech, GlaxoSmithKline, Guthy-Jackson/GGF, Immunic, Janssen/Actelion, MAPI, Medimmune, Merck/EMD Serono, Novartis, Ono Pharmacia, Roche/Genentech, Sanofi-Genzyme, Teva Neuroscience, Wyeth (consulting fee). Bruce A C Cree: Akili, Alexion, Atara, Biogen, EMD Serono, Novartis, TG Therapeutics (consulting fee). Le H. Hua: Biogen, Celgene, EMD Serono, Genentech, Genzyme, Novartis (consulting fee). Amos Katz: Biogen, Genentech, Novartis, Sanofi (consulting fee). Derrick Robertson: Acorda (speakers bureau). Actelion, MedDay, Medimmune, PCORI, TG Therapeutics (grant support). Alexion, Celgene, Teva Neuroscience (consulting fee, speakers bureau). Biogen, EMD Serono, Genentech, Novartis, Sanofi-Genzyme (consulting fee, grant support, speakers bureau). Mallinckrodt (grant support, speakers bureau). Brandon Brown, Desiree Dunlop, Xiangyi Meng, Wendy Su: Novartis Pharmaceuticals Corporation (salary).*

Keywords: Disease-modifying treatments in MS

(DXT05)

Efficacy of Diroximel Fumarate in Highly Active Relapsing-Remitting Multiple Sclerosis: Interim Results from the Phase 3 Evolve-MS-1 Study

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Background: Diroximel fumarate (DRF) is a novel oral fumarate recently approved in the United States for relapsing forms of multiple sclerosis (MS). Currently, there are no published data demonstrating the efficacy of DRF in patients with highly active relapsing-remitting MS (RRMS). Increased frequency of relapses and high MRI lesion load are associated with an increased risk of MS progression.

Objectives: To evaluate clinical and radiological efficacy of DRF in patients with highly active RRMS.

Methods: EVOLVE-MS-1 (NCT02634307) is an ongoing, open-label, Phase 3 study of long-term safety, tolerability, and treatment effect of DRF over 96 weeks in adults with RRMS. Efficacy outcomes were assessed in a post-hoc subgroup analysis of patients from EVOLVE-MS-1 with highly active RRMS (≥2 relapses in the year before study entry and ≥1 gadolinium-enhancing [Gd+] lesion at baseline). Assessments included adjusted annualized relapse rate (ARR), Gd+ lesion count, and 12-week confirmed disability progression (CDP; ≥1.5-point increase in Expanded Disability Status Scale score from a baseline score of 0, or a ≥1-point increase from a baseline score of 1.0–5.5, sustained for 12 weeks).

Results: A total of 57 patients with highly active RRMS were enrolled in EVOLVE-MS-1 as of 30 November 2018, 14 of whom were newly diagnosed and naïve to disease-modifying therapy. Patients had a mean (SD) time since diagnosis of 4.2 (4.6) years and 2.2 (0.6; range 2-5) relapses in the 12 months before study entry. Median (range) DRF exposure for the highly active subgroup was 84 (1–100) weeks; 72% of patients were on treatment for ≥1 year. Adjusted ARR was reduced by 83.3% (95% CI 72.0–90.7; $p<0.0001$) with DRF treatment compared with the 12 months before study entry (0.36 [95% CI 0.20–0.65] vs 2.22 [95% CI 2.06–2.40]), and 73.7% of patients were relapse-free. Estimated proportion of patients with 12-week CDP at Week 48 was 8.3%. Mean (SD) time to disability progression for patients who progressed was 5.4 (4.8) months. Significant reductions in mean (SD) Gd+ lesion counts were observed at Week 48 (1.0 [4.7]; n=41) compared with baseline (5.0 [7.7]; n=53; 80% reduction; $p=0.0003$), and a greater percentage were Gd+ lesion-free (Week 48: 80.5% vs baseline: 9.4%).

Conclusions: DRF demonstrated notable benefits on clinical and radiological outcomes in patients with highly active RRMS. These data and comparison with similar cohorts (DEFINE/CONFIRM highly active RRMS) support DRF as a treatment option for MS patients with active disease.

Support: Biogen

Disclosure: *Annette Wundes: Alkermes, AbbVie, and Biogen (contracted research). Biogen (consulting fee). Enrique Alvarez: Actelion, Biogen, Celgene, EMD Serono, Genentech, Genzyme, Novartis, Teva, and TG Therapeutics (consulting fee). Biogen, Genentech, Novartis, and Rocky Mountain MS Center (contracted research). Mark S. Freedman: Actelion, Bayer, Biogen, Celgene, Chugai, EMD Canada, Genzyme, Merck Serono, Novartis, Hoffman La-Roche, PENDOPHARM, and Sanofi-Aventis (consulting fee). Actelion, Bayer, Biogen, Clene, Hoffman La-Roche, Merck Serono, MedDay, Novartis, and Sanofi-Aventis (participation as a member in a company advisory board, board of directors, or other similar group). Genzyme Canada (contracted research). Sanofi-Genzyme (speakers bureau). Oksana Mokliatchouk, Hailu Chen, Shivani Kapadia, Jordan Messer: Biogen (ownership interest, salary). Robert T. Naismith: Alexion, Alkermes, Biogen, Celgene, EMD Serono, Genentech, Novartis, Sanofi Genzyme, TG Therapeutics, and Viela Bio (consulting fee).*

Keywords: Disease-modifying treatments in MS, Highly Active Disease

(DXT06)

Real-World Effectiveness of Peginterferon Beta-1a Versus Interferon Beta-1a and Glatiramer Acetate in US MS Patients

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Background: Interferons (IFNs) and glatiramer acetate (GA) are effective in reducing relapses in relapsing-remitting multiple sclerosis (RRMS). Matching-adjusted indirect comparisons and propensity score (PS) matching analyses of clinical trial data have evaluated the efficacy of disease-modifying therapies (DMTs). However, studies evaluating their real-world effectiveness are limited.

Objectives: To compare clinical outcomes, effectiveness and healthcare resource measures for patients with multiple sclerosis (MS) initiating subcutaneous (SC) peginterferon beta-1a, SC IFN beta-1a three times weekly (SC IFN), or GA in routine clinical practice.

Methods: This retrospective, observational comparative effectiveness study used data from the Truven MarketScan® Commercial Claims Database. Patients aged 18-65 years presenting at least one claim for an MS diagnosis were selected if they initiated peginterferon beta-1a, SC IFN, or GA between November 2014 and March 2017 as standard of care. PS was derived from baseline characteristics and patients were PS matched, including 685 patients for peginterferon beta-1a vs. 2035 for SC IFN, and 858 for peginterferon beta-1a vs. 2573 for GA. Demographic, clinical and healthcare resource measures were evaluated at baseline and post-index measures were evaluated. Annualized relapse rates (ARRs) were compared using a negative binomial model adjusting for disease duration and prior DMTs. The index date was the first peginterferon beta-1a claim, the first SC IFN claim, or the first GA claim.

Results: Prior DMT utilization was higher with peginterferon beta-1a vs. SC IFN (75.1% vs. 15.2%, $p<0.0001$), and with peginterferon beta-1a vs. GA (75.1% vs. 13.3%, $p<0.0001$). The

mean persistence of time a patient was on peginterferon beta-1a (post-index date) was 483 days for the SC IFN comparison and 497 days for the GA comparison. After adjusting for baseline patient demographics and clinical characteristics and PS matching, ARR during the post-index period was lower with peginterferon beta-1a than with SC IFN (0.18 vs. 0.23, relative risk [RR]=0.795, p=0.02). There was a trend toward decreased ARR with peginterferon beta-1a vs. GA (0.20 vs. 0.23, RR=0.876, p=0.18).

Conclusions: ARR was lower with peginterferon beta-1a than with SC IFN, and a trend toward decreased ARR with peginterferon beta-1a vs. GA was observed. These real-world results contribute to the data available for decision-making in routine clinical practice.

Support: Biogen

Disclosure: *Anthony T. Reder: Bayer, Biogen, Novartis, Serono (unrestricted grant support and/or advisory board compensation for my work). Nancy Arndt: Biogen, Genzyme, Novartis, Teva (consulting, advisory board compensation, and/or compensation for speaking). Caroline Geremakis, Jason P. Mendoza, Ray Su, Charles Makin, Megan C. Vignos, Robin Avila: Biogen (employee of, and may hold stock and/or stock options in, biogen).*

Keywords: Disease-modifying treatments in MS, real-world evidence

(DXT07)

Injection Site Reactions and Risk of Discontinuation Among New and Experienced Peginterferon Beta-1a Users in the Plegridy Observational Program

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Background: Injection site reactions (ISRs) are a common adverse event associated with peginterferon beta-1a treatment and may lead to discontinuation. This analysis of the Plegridy Observational Program (POP), a 5-year, phase 4 real-world study, assessed the relationship between ISRs and discontinuation of peginterferon beta-1a.

Objectives: Assess the risk of treatment discontinuation associated with ISRs in new and experienced users of peginterferon beta-1a.

Methods: Using POP 3rd interim data from November 2014 to September 2018, patients were classified as new users if they initiated peginterferon beta-1a ≤31 days prior to, on, or after study consent; and experienced users if they initiated peginterferon beta-1a >31 days prior to study consent. Treatment discontinuation was based on physician report and only the first discontinuation was analyzed. Demographics and baseline characteristics were summarized with descriptive statistics. Frequencies and proportions of individuals who experienced ≥1 ISR were

calculated for each group. Fisher exact test assessed the relative risk (RR) of discontinuation in those with or without ISRs. Kaplan-Meier analysis assessed the cumulative risk of discontinuation. Data from the 4th interim POP analysis (as of September 2019) will be presented.

Results: Of the 1126 patients included in this analysis, 576 (51%) were new and 550 (49%) were experienced users of peginterferon beta-1a. Among new and experienced users, 280 (49%) and 147 (27%) reported ≥1 ISR, respectively. In the new-user cohort, 148 (53%) patients with ISRs and 135 (46%) patients without ISRs discontinued peginterferon beta-1a treatment (RR: 1.16 [95% confidence interval (CI): 0.98, 1.37]). In experienced users, 44 (30%) patients with ISRs and 124 (31%) patients without ISRs discontinued peginterferon beta-1a treatment (RR: 0.97 [95% CI: 0.73, 1.30]). Over 12 months of treatment in the new-user cohort, the cumulative probability of peginterferon beta-1a discontinuation was 0.38 in patients with ≥1 ISR and 0.31 in patients without an ISR.

Conclusions: These preliminary findings suggest an increased risk of discontinuation in new users of peginterferon beta-1a with ISRs, whereas in experienced users no impact of ISRs on discontinuation was observed. New users of peginterferon beta-1a treatment may benefit from additional information on ISR mitigation and management through discussions with their health care professionals.

Support: Biogen

Disclosure: *Ayo Adeyemi, Nicole Tsao, Arman Altincatal, Maria L. Naylor, Charles Makin: Biogen (employee of, and may hold stock and/or stock options in, biogen). Marco Salvetti: Biogen, Merck, Novartis, Roche, Sanofi, Teva (received grant support and/or speaker honoraria). Sibyl Wray: Bayer, Biogen, Celgene, EMD Serono, Genentech/Roche, Genzyme/Sanofi, Novartis, Receptos, TG Therapeutics (paid consultant, speaker, and/or contract researcher). Gereon Nelles: Bayer, Biogen, Celgene, Merck, Novartis, Roche (received speaker honoraria).*

Keywords: Disease-modifying treatments in MS, injection site reactions

(DXT08)

Post Hoc Analysis of Efficacy of Cladribine Tablets in Patients with Relapsing-Remitting Multiple Sclerosis Diagnosed within 3 or 4 Years Prior to the Clarity Study

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Background:
Cladribine tablets 3.5 mg/kg (CT3.5, cumulative dose over 2 years; N=433) treatment significantly improved clinical and magnetic resonance imaging (MRI) outcomes vs placebo (PBO; N=437) in relapsing-remitting multiple sclerosis (RRMS) in the 96-week (wk) CLARITY study. Prior *post hoc* analyses of CLARITY found that patients with shorter disease duration (<3 years) responded more favorably to CT3.5 in risk reduction of relapse and odds of achieving disease-free activity status vs those with longer disease duration (≥3 years). Further analyses are needed to assess the extent of benefit of CT3.5 in patients with a relatively shorter disease duration.

Objectives:
This *post hoc* analysis further examined efficacy outcomes in CLARITY patients who were early in their disease course (<3 or <4 years newly diagnosed [YND]) at study enrollment.

Methods:
Analyses were performed by treatment (CT3.5 vs PBO) and MS-duration groups (<3 YND, <4 YND at CLARITY enrollment). Endpoints were relapse, 3- and 6-month (mo) confirmed disability progression (CDP, based on Expanded Disability Status Scale), MRI activity, and No Evidence of Disease Activity (NEDA) status (no relapse, CDP, or MRI activity). P-values are nominal.

Results:
These MS-duration group analyses were carried out in 492 patients: <3 YND: CT3.5 N=228, PBO N=207; <4 YND: CT3.5 N=256, PBO N=236. In both MS-duration groups, CT3.5 significantly reduced annualized relapse rate (<3 YND: 0.14 vs 0.37 [60.7% reduction]; <4 YND: 0.14 vs 0.36 [61.6% reduction]; P<0.0001), and increased the number of patients who were relapse-free through Wk 96 (<3 YND: 75.4% vs 55.1%; <4 YND: 75.0% vs 55.9%) vs PBO. CT3.5 treatment increased the probability of being free from 3- or 6-mo CDP through Wk 96 (3-mo CDP at Wk 96 in both groups: 0.84–0.85 vs 0.76 [both groups]; 6-mo CDP at Wk 96: 0.89–0.90 vs 0.83–0.84) vs PBO. CT3.5 also significantly reduced the adjusted mean (95% confidence interval) cumulative number of new T1 gadolinium-enhancing (<3 YND: 0.11 [0.08–0.16] vs 1.0 [0.73–1.36]; <4 YND: 0.11 [0.08–0.16] vs 0.93 [0.69–1.24]) and active T2 (<3 YND: 0.41 [0.33–0.51] vs 1.68 [1.36–2.06]; <4 YND: 0.41 [0.33–0.50] vs 1.63 [1.34–1.97]) lesions, and increased the number of patients achieving NEDA status using 3-mo (<3 YND: 40.4% vs 11.1%; <4 YND: 39.5% vs 11.4%) or 6-mo (<3 YND: 41.2% vs 11.6%; <4 YND: 40.2% vs 12.3%) CDP vs PBO (all P<0.0001) at 96 wks.

Conclusions:
Overall, CT3.5 treatment improved clinical and MRI outcomes in CLARITY patients who were early in their disease course.

Disclosure: *Barry Singer: AbbVie, Biogen, Novartis, Roche, Sanofi Genzyme (consulting fee, research support). Alexion, Bayer, Celgene, EMD Serono, Genentech, Teva, TG Therapeutics (consulting fee). Alkermes, Medimmune (research support). Gavin Giovannoni: Abbvie, Actelion, Almirall, Atara Bio, Bayer Schering Pharma, FivePrime, GlaxoSmithKline, GW Pharma, Merck KGaA, Pfizer Inc, Protein Discovery Laboratories, Sanofi-Genzyme, Teva Pharmaceuticals Industries Ltd, UCB, Vertex Pharmaceuticals (consulting fee). Biogen Idec, Ironwood, Merck and Co, Novartis (consulting fee, unrelated research support). Nicola De Stefano: BayerSchering AG, Merck Serono S.A, Novartis Pharma AG, Sanofi-Aventis, Serono Symposia International Foundation, Teva Pharmaceutical Industries (consulting fee). Matt Mandel, Julie Aldridge, Caroline Lemieux: EMD Serono, Inc. (a business of Merck KGaA, Darmstadt, Germany) (salary). Yann Hyvert: Merck KGaA (salary). Andrew Galazka: Merck KGaA, Aubonne, Switzerland (a business of Merck KGaA, Darmstadt, Germany) (salary). Mark S. Freedman: Actelion, Bayer HealthCare, Biogen Idec, Chugai, EMD Canada, Genzyme, Hoffman La Roche, Novartis, Sanofi, Teva (consulting fee).*

Keywords: Disease-modifying treatments in MS

(DXT09)

Exploration of Factors Which Influence Treatment Decisions of Patients with Multiple Sclerosis

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Background: The past ten years have brought a wide variety of therapeutic options to Australian patients with Relapsing Remitting Multiple Sclerosis (RRMS). In a complex treatment landscape for an unpredictable disease, it's important to understand how patients view the various factors that contribute to making an informed therapeutic choice.

Objectives: Identify the factor rated by Patients with RRMS (PwRRMS) as having the most influence on treatment choice.

Methods: This non-interventional, exploratory study prospectively enrolled 78 patients assigned to one of three groups:

1. Initial treatment (n=25)
2. Switching to alternate treatment (n=27)
3. Stable on treatment (n=26)

Baseline demographic and MS data was collected. Participants completed the survey where they rated factors from most to least important: Drug safety; Efficacy; Ease of use; Mode of administration; Mechanism of action; Concern about disability; Requirement for follow-up safety monitoring; Balance of risk/benefit; Value of discussion with MS nurse & neurologist.

Results: The factors ranked first by most participants in influencing treatment choice were (in order):

1. Concern about disability (31/78 participants)
2. Perception of efficacy (16/78)
3. Perception of safety (11/78)

This ranking order was consistent across all groups. 97% of participants were satisfied with the process around choosing treatment and 92% reported they felt extremely comfortable with their treatment decision.

Conclusions: Our data indicates that concern about disability is the largest driving factor for PwRRMS choosing between treatments regardless of whether they are starting for the first time, planning a switch in therapy or are currently stable on an MS medication.

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Keywords: Comprehensive care and MS, Disease-modifying treatments in MS, Nursing management in MS

(DXT10)

Siponimod Affects Disability Progression in Patients with SPMS Independent of Relapse Activity: Results from the Phase 3 Expand Study

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Background: Siponimod (Mayzent®) is a selective sphingosine 1-phosphate receptor ($S1P_1$, $S1P_5$) modulator, approved in the USA for the treatment of relapsing forms of multiple sclerosis (MS), including active secondary progressive MS (SPMS). In the phase 3, randomized, double blind, placebo controlled EXPAND trial, siponimod reduced the risk of 3- and 6-month (m) confirmed disability progression (CDP) by 21% and 26%, respectively, compared with placebo, in patients with SPMS. Subgroup analyses of EXPAND data suggest that a proportion of the effect of siponimod on CDP was attributable to effects on relapse-independent disability progression.

Objectives: Assess the impact of siponimod on CDP in patients with/without relapses to uncouple treatment effects on CDP from those on relapses.

Methods: In EXPAND, patients (aged 18-60 years) with SPMS and Expanded Disability Status Scale score of 3.0-6.5 were included in the study and received once-daily oral siponimod 2 mg or placebo for up to 3 years. We analysed the impact of siponimod on CDP by subgroup analysis using the Cox model on time to 3m- and 6m-CDP in patients with or without relapses in the 1- and 2-years before study; principal stratum analysis to estimate the effect in patients who would not have relapsed on-study at the m12, m18 and m24 timepoints, regardless of treatment; and Cox model on time to 3m/6m-CDP in the overall population, censoring at time of first relapse.

Results: For non-relapsing patients in 1- and 2-years before study, risk reductions were 18% (hazard ratio [HR], 0.82 [confidence interval (CI):0.66; 1.02]) and 13% (0.87 [0.68; 1.11]), respectively, for 3m-CDP, and 25% (0.75 [0.59; 0.96]) and 18% (0.82 [0.62; 1.08]), respectively, for 6m-CDP; for relapsing patients, risk reductions were 33% and 33% (3m-CDP), and 30% and 37% (6m-CDP), respectively. In principal stratum estimates, siponimod reduced 3m-CDP by 14-20% and 6m-CDP by 29-33% in non-relapsing patients across the 3 timepoints, suggesting that these patients achieved a large proportion of the effect in the overall population. Cox model censoring at relapse confirmed beneficial effects, reaching nominal statistical significance (6m-CDP: HR 0.77 [0.62;0.96]).

Conclusions: Siponimod reduces risk of CDP in SPMS patients with or without relapses, indicating that the effects on disability are largely independent from those on relapses. Patients with or without relapses may thus benefit from treatment with siponimod.

Disclosure: *Bruce A C Cree: Akili, Alexion, Atara, Biogen, EMD Serono, Novartis, TG Therapeutics (consulting fee). Robert J. Fox: Actelion, EMD Serono, Genentech, Teva (consulting fee). Biogen, Novartis (consulting fee, contracted research). Gavin Giovannoni: AbbVie, Bayer-Schering, Biogen, Canbex, Eisai, Elan, Five Prime, Genentech, Genzyme/Sanofi, GlaxoSmithKline, GW Pharmaceuticals, Ironwood, Merck Serono, Novartis, Pfizer, Roche, Synthon BV, Teva (consulting fee). Multiple Sclerosis and Related Disorders (Elsevier) (serving as co-chief editor). UCB Pharma (grants). Patrick Vermersch: Bayer HealthCare, Biogen Idec, Merck Serono, Novartis, Teva Neuroscience (consulting fee, research support). Celgene, Roche, Sanofi, Servier (consulting fee). SAGE, Thieme Verlag (serving as an editor). Amit Bar-Or: Atara Biotherapeutics, Bayer, Bayhill Therapeutics, Berlex, Biogen*

Idec, BioMS, Celgene/Receptos, Diogenix, Eli Lilly, F Hoffman-La Roche, Genentech, GlaxoSmithKline, Guthy-Jackson/GGF, Immunic, Janssen/Actelion, MAPI, Medimmune, Merck/EMD Serono, Novartis, Ono Pharmacia, Roche/Genentech, Sanofi-Genzyme, Teva Neuroscience, Wyeth (consulting fee). Ralf Gold: Bayer HealthCare, Biogen Idec, Merck Serono, Novartis, Teva Neuroscience (consulting fee, contracted research). SAGE, Thieme Verlag (personal fees for serving as an editor). Nicolas Rouyrre, Goeril Karlsson, Frank Dahlke: Novartis Pharma AG (salary). Ludwig Kappos: Actelion, Alkermes, Allergan, Almirall, Bayer, Biogen, Celgene, CSL Behring, df-mp, European Union, EXCEMED, GeNeuro, Genzyme, Merck, Mitsubishi Tanabe Pharma, Novartis, Pfizer, Receptos/Celgene, Roche, Roche Research Foundations, Sanofi-Aventis, Santhera, Swiss Multiple Sclerosis Society, Swiss National Research Foundation, Teva, UCB Pharma, Vianex (contracted research). Neurostatus products (license fees).

Keywords: Disease-modifying treatments in MS

(DXT11)

The Implications of Suboptimal Treatment Outcomes with Disease-Modifying Drugs in Employees with Multiple Sclerosis

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Background: A better understanding of the implications of suboptimal treatment outcomes in employees with multiple sclerosis (MS) may elucidate opportunities for improving care management.

Objectives: To evaluate suboptimal treatment outcomes with disease-modifying drugs (DMD) in patients with MS from an employer perspective.

Methods: US Human Capital Management Services database employees were eligible if they had: ≥2 claims with MS diagnoses (ICD-9 CM 340.xx/ICD-10 CM G35) from 1/1/2010–3/31/2019, ≥1 once-/twice-daily oral or any self-injectable DMD claim (first claim=index), continuous eligibility 6-months pre- (baseline) and 1-year post-index (follow-up), no baseline DMD, age 18–64. Suboptimal treatment outcomes were DMD nonadherence (proportion of days covered <80%), DMD discontinuation (treatment gap >60 days), DMD switch, or relapse (MS-related hospitalization, emergency room visit, or outpatient visit with corticosteroid ±7 days). A two-part logistic-GLM model evaluated costs controlling for age, tenure, marital status, race, exempt status, full-/part-time, salary, location, Charlson Comorbidity Index, smoking, and relapse.

Results: Of 2173 employees with ≥2 MS diagnoses, 488 (22.5%) met eligibility. Half (n=247; 50.6%) had suboptimal treatment outcomes (39.5% nonadherence, 9.8% discontinuation, 10.9%

switching, 20.7% relapse; indicators not mutually exclusive). Baseline characteristics were similar for employees with vs without suboptimal treatment outcomes: mean age: 42.60 vs 43.87; female: 73.7% vs 71.4%; white/black/Hispanic: 32.0%/5.3%/3.6% vs 29.5%/5.8%/6.6%; married: 23.1% vs 27.4%; mean salary: $61,898 vs $68,737; hypertension: 14.6% vs 16.6%; hyperlipidemia: 11.7% vs 12.9%; gastrointestinal disease: 16.6% vs 12.9%; tobacco use: 3.2% vs 2.5%; baseline magnetic resonance imaging: 57.9% vs 58.9%; baseline relapse: 22.7% vs 19.9%. Employees with vs without suboptimal treatment outcomes had higher all-cause medical ($12,730 vs $6428; p<0.0001), MS-related medical ($5444 vs $2652; p<0.0001), non-DMD pharmacy ($2920 vs $2169; p=0.0199), sick leave ($1247 vs $908; p=0.0274), and short-term disability ($934 vs $146; p=0.0001) costs. Long-term disability ($751 vs $0; p=0.1250) and Workers' Compensation ($56 vs $24; p=0.1276) costs did not differ significantly.

Conclusions: Half of employees with MS had suboptimal 1-year treatment outcomes (nonadherence, discontinuation, switching, relapse). Suboptimal response to DMD treatment was associated with higher medical, sick leave, and short-term disability costs.

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(DXT12)

Real-World Effectiveness of Peginterferon Beta-1a Versus Teriflunomide in US MS Patients

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Background: Both peginterferon beta-1a and teriflunomide (TERI) have been shown in clinical studies to effectively reduce relapses in relapsing-remitting multiple sclerosis (RRMS). In lieu of head-to-head studies, efficacy comparisons between disease modifying therapies (DMTs) can be assessed through matched-adjusted indirect comparisons and propensity score (PS) matching. However, real-world studies are also valuable in demonstrating the differences in the effectiveness of multiple sclerosis (MS) DMTs.

Objectives: To compare clinical outcomes and effectiveness for patients with MS initiating subcutaneous (SC) peginterferon beta-1a and TERI in routine clinical practice.

Methods: Utilizing the Truven MarketScan® Commercial Claims Database, a retrospective, observational comparative effectiveness study was performed. Patients aged 18-65 years presenting at least one claim for an MS diagnosis were selected if they were initiated on peginterferon beta-1a or TERI between November 2014 and March 2017 as standard of care. PS was derived from the baseline characteristics and patients were PS matched, including 704 patients for peginterferon beta-1a vs. 2099 for TERI. Demographic, clinical and healthcare resource measures were evaluated at baseline and post-index measures were evaluated. Annualized relapse rate (ARRs) were compared using a negative binomial model adjusting for disease duration and number of prior DMTs. The index date was the first claim for peginterferon beta-1a or TERI, for each respective cohort.

Results: Significant differences in prior DMT utilization were observed between the peginterferon beta-1a vs. TERI cohorts (77.5% vs 56.9%, p=0.0005). After adjustment for baseline patient demographics and clinical characteristics and PS matching, there was a significant difference in ARR during the post-index period between peginterferon beta-1a-treated and TERI-treated patients (0.26 vs. 0.33, p=0.0003).

Conclusions: Statistically significant differences in ARR between peginterferon beta-1a and TERI were observed. These findings from real-world data help support decision-making in routine clinical practice.

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(DXT13)

Disease Modifying Therapies: How Confident Are We That We Understand Their Risk?

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Background:

An increasing number of therapeutic options are available for multiple sclerosis (MS) patients. Each medication has a unique efficacy and safety profile that needs to be critically evaluated in order to optimize the risk and benefit for each patient's individual treatment plan. While most efficacy data are obtained in Phase III trials, safety profiles may change over time as patients

utilize these medications in a real-world setting. Participants in clinical trials are often younger and have less co-morbidities than the general MS population. In order to understand the evolving nature of serious adverse events (SAEs), it is important to have up-to-date information on the incidence of these events balanced by the number of patients exposed to the medication, as well as the patient years exposure.

Objectives: To compare rates of SAEs for approved MS disease modifying therapies in relation to current patient exposures and patient years of exposure.

Methods:

A retrospective analysis was performed to obtain SAE data from the manufactures of the most commonly prescribed MS medications.

Results:

As of the writing of this abstract, cases of progressive multifocal leukoencephalopthy (PML) have been reported by natalizumab (825), fingolimod (30), dimethyl fumarate (8), ocrelizumab (8), teriflunomide (1), and alemtuzumab (1). 45 cases of cryptococcal meningitis have occurred with fingolimod. Multiple cases of Steven's Johnson and a single fatal case of toxic epidermal necrolysis has been reported with teriflunomide. 13 cases of ischemic and hemorrhagic stroke or arterial dissection have been reported with alemtuzumab. This led to a recent update and boxed warning in the US prescribing information for alemtuzumab. The approximate number or patients exposed to alemtuzumab prior to this update was approximately 22,000, representing approximately 45,000 patient years.

Conclusions:

These findings suggest that newly approved medications may require 20,000+ patients with 40,000+ patient years to uncover serious adverse events in the real-world setting. Current patient exposures for injectable, oral, and infusible MS medications range from 2,000 to over 500,000 while patient years range from 10,000 to over 2.5 million. A comparison of the above (and additional) SAE rates by patient exposure will be presented.

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(DXT14)

Long-Term Safety and Efficacy of Eculizumab in Neuromyelitis Optica Spectrum Disorder

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Background: Neuromyelitis optica spectrum disorder (NMOSD) relapses can cause significant and irreversible neurologic disability. Eculizumab, a terminal complement inhibitor, reduces the risk of NMOSD relapse in patients with aquaporin-4 immunoglobulin G (AQP4-IgG)-positive NMOSD. In the PREVENT study, eculizumab reduced the risk of relapse by 94.2% versus placebo (hazard ratio 0.058; 95% confidence interval [CI]: 0.017, 0.197; $p < 0.0001$). The rate of adverse events (AEs)/100 patient-years (PY) was 749.3 and 1160.9 for eculizumab and placebo, respectively.

Objectives: To present combined long-term safety and efficacy data for eculizumab from the randomized, double-blind, placebo-controlled PREVENT study (NCT01892345) and its ongoing open-label extension (OLE) (NCT02003144) in patients with AQP4-IgG-positive NMOSD.

Methods: Patients with AQP4-IgG-positive NMOSD received eculizumab 1200 mg/2 weeks (maintenance dose). Eculizumab safety and efficacy data from the PREVENT and OLE studies (data cut-off: October 31, 2018) were combined.

Results: Overall, 137 patients received eculizumab. These patients were followed for a median of 107.9 (range 5.1–237.9) weeks and a combined total of 282.3 PY after eculizumab initiation. The rates of AEs and serious AEs (SAEs) per 100 PY were 763.1 and 37.6, respectively. The most common AEs included headache (27.0%), upper respiratory tract infection (25.5%), nasopharyngitis (22.6%), urinary tract infection (16.8%), nausea (16.1%), back pain (15.3%) and diarrhea (15.3%). Common SAEs, excluding NMOSD relapses, were pneumonia (2.9%), urinary tract infection (2.9%) and optic neuritis (2.2%). There was one death during PREVENT (pulmonary empyema) and one patient developed *Neisseria gonorrhoeae* infection in the OLE. No patient had a meningococcal infection. In total, 8/137 (5.8%) patients treated with

eculizumab experienced an adjudicated on-trial relapse; an estimated 93.9% (95% CI: 87.5, 97.1) of patients were relapse-free at 192 weeks.

Conclusions: In this long-term analysis, eculizumab was well tolerated and reported AEs were consistent with its established safety profile in other indications. The percentage of relapse-free patients remained high (approximately 94%) through 192 weeks.

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Keywords: Long-Term Safety and Efficacy of Eculizumab in NMOSD

(DXT15)

Inebilizumab Reduces Neuromyelitis Optica Spectrum Disorder Disability Worsening: Outcomes and Long-Term Follow-up Data from the N-Momentum Trial

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Background: Neuromyelitis optica spectrum disorder (NMOSD) is a rare, relapsing, autoimmune, inflammatory disease of the central nervous system. Disability accumulates with repeated attacks, severely impacting quality of life. Inebilizumab, an anti-CD19 monoclonal B-cell-depleting antibody, was assessed in N-MOmentum, a randomized, placebo-controlled, double-masked trial in patients with NMOSD.

Objectives: To assess the effectiveness of inebilizumab on disability outcomes in N-MOmentum and determine if severity of pre-existing disability influenced efficacy.

Methods: Adults with NMOSD and an Expanded Disability Status Scale (EDSS) score ≤8 were randomized 3:1 to receive inebilizumab 300mg or placebo on days 1 and 15. The randomized controlled period (RCP) was 28 weeks or up to an adjudicated attack. The proportion of patients with disability worsening (EDSS score change ≥2 from a baseline of 0, ≥1 from a baseline of 1–5, or ≥0.5 from a baseline of ≥5.5) was assessed by logistic regression. Change from baseline in modified Rankin scale (mRS) scores was analyzed by the Wilcoxon–Mann–Whitney odds approach. Subgroup analysis by baseline EDSS score of the primary outcome (time to adjudicated attack) was performed by Cox proportional hazards regression.

Results: The median (range) baseline EDSS of the 174 patients receiving inebilizumab was 3.5 (0–8) and 4.0 (1–8) for the 56 receiving placebo; 18.0% and 30.4% had disability worsening at Week 12, respectively. At the end of RCP, 15.5% of patients on inebilizumab and 33.9% on placebo had disability worsening; odds ratio (95% confidence interval [CI]): 0.370 (0.185–0.739); p=0.0049. Of the 9632 paired comparisons, mRS outcomes at end of RCP were better with inebilizumab than placebo in 51.5% of cases and were equal in 21.9% of cases; adjusted odds ratio (95% CI): 1.663 (1.195–2.385); p=0.0023. Inebilizumab reduced the risk of attack compared with placebo in patients with baseline EDSS in the lower (<5) or upper half (≥5) of the 10-point scale; hazard ratios (95% CI): 0.257 (0.120–0.552); p=0.0005 and 0.367 (0.137–0.981); p=0.0456, respectively; the treatment effect was not significantly different (interaction test, p=0.6363). Long-term, open-label follow-up data will be presented.

Conclusions: In N-MOmentum, disability outcomes were significantly better with inebilizumab monotherapy than with placebo. Inebilizumab reduced the risk of attack in patients with NMOSD irrespective of the level of pre-existing disability.

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(DXT16)

Effectiveness of Delayed-Release Dimethyl Fumarate Relative to Duration of Prior GA in Patients Enrolled in the Respond Study

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Background: Dimethyl fumarate (DMF) has demonstrated efficacy and a favorable benefit–risk profile in clinical studies of patients with relapsing-remitting multiple sclerosis (RRMS). RESPOND (NCT01903291), a phase 4, 12-month study, evaluated outcomes in patients with RRMS prescribed DMF after suboptimal response to glatiramer acetate (GA). Patients may experience a suboptimal response to a disease modifying therapy such as GA early after treatment initiation, or in some cases, after several years.

Objectives: To evaluate relapse and patient-reported outcomes (PROs) over 12 months in RRMS patients who switched to DMF after suboptimal response to GA in real-world practice and to explore whether time on prior GA may influence response to DMF.

Methods: RESPOND was conducted at 63 sites in the US between August 2013 and February 2016. Patients diagnosed with RRMS with a suboptimal response to GA (perceived insufficient efficacy, intolerance, or poor adherence to GA) were enrolled. The median duration of prior GA was 36 months. This post-hoc analysis compared treatment outcomes at 12 months following DMF initiation in subgroups of patients according to duration of prior GA treatment (≤36 months vs >36 months).

Results: Among patients treated with GA for ≤36 months (n=177) and >36 months (n=141), the ARR at 12 months prior to DMF was 0.588 (95%CI 0.49–0.70), and 0.369 (95%CI 0.28–0.49), whereas 12 months after switching to DMF, the ARR was 0.094 (95%CI 0.05–0.18), and 0.121 (95%CI 0.07–0.22), respectively (ARR reductions of 84% and 67%, respectively). The estimated proportion of patients relapsed (PPR) at Month 12 on DMF was 6.5% for patients who had received prior GA for ≤36 months and 9.8% for patients who had received prior GA for >36 months. PROs for quality of life, fatigue, disability, treatment satisfaction, work productivity,

and depressive symptoms improved or remained stable in both subgroups. We will also present outcomes for subgroups stratified by reason for discontinuation (insufficient efficacy vs other).

Conclusions: Improvements in ARR and PPR were observed in patients who switched to DMF earlier (<36 months prior GA treatment), and in patients who switched to DMF after being treated with GA for >36 months. ARR and PPR were numerically lower in the group who switched earlier, but these differences were not statistically significant between the two subgroups. Both groups demonstrated improvement or stability across several PROs.

Support: Biogen

Disclosure: *Derrick Robertson: Acorda (speakers bureau). Actelion, MedDay, PCORI, TG Therapeutics (contracted research). Alexion, Celgene, Teva Neuroscience (consulting fee, speakers bureau). Biogen, EMD Serono, Genentech, Novartis, Sanofi-Genzyme (consulting fee, contracted research, speakers bureau). Mallinckrodt (contracted research, speakers bureau). Pavle Repovic: Alexion (consulting fee, speakers bureau). Biogen, EMD Serono (consulting fee, contracted research, speakers bureau). Celgene, Novartis, Sanofi-Genzyme, Viela (consulting fee). Genentech (contracted research, speakers bureau). Genzyme (speakers bureau). Stanley L. Cohan: AbbVie, Adamas, Alexion, Alithios, MedDay, Pear Therapeutics, Roche Genentech, Sage Therapeutics (contracted research). Biogen, Novartis (consulting fee, contracted research, speakers bureau). EMD Serono, Roche (consulting fee). Genentech (consulting fee, speakers bureau). Sanofi Genzyme (consulting fee, contracted research). Sanofi-Genzyme, Teva Neuroscience (speakers bureau). Yang Mao-Draayer: Bayer Pharmaceutical, Celgene, EMD Serono, Genentech, Teva (consulting fee). Biogen, Sanofi-Genzyme (consulting fee, contracted research). Chugai, NIAID Autoimmune Center of Excellence UM1-AI110557, NIH NINDS R01-NS080821, Novartis (contracted research). Ray Su, James B. Lewin: Biogen (ownership interest, salary). Jenna Borowski: Biogen (salary).*

Keywords: Dimethyl fumarate, Disease-modifying treatments in MS

(DXT17)

Long-Term Follow-up Results from the Phase 2 Multicenter Study of Ublituximab (UTX), a Novel Glycoengineered Anti-CD20 Mab, in Patients with RMS

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Background: UTX is a novel mAb targeting a unique epitope on the CD20 antigen and glyco-engineered for enhanced B-cell targeting through antibody-dependent cellular cytotoxicity (ADCC). Two Phase III trials, ULTIMATE I and II, are fully enrolled and are investigating the efficacy and safety of UTX in RMS.

Objectives: To evaluate the long-term safety and tolerability of ublituximab (UTX) treatment in patients with relapsing forms of multiple sclerosis (RMS) enrolled in the Open Label Extension (OLE) of a phase 2 trial.

Methods: TG1101-RMS201 was a 52-week, phase 2, placebo-controlled, multicenter study of UTX in RMS. Subjects who completed RMS201 were eligible to continue treatment in the OLE, receiving one-hour 450mg UTX infusions every 24 weeks.

Results: RMS201 enrolled 48 subjects and the primary endpoint was to evaluate B-cell depletion. Median B-cell depletion of >99% was observed at Week 4 and maintained at Week 48. At Week 48, key observations included: 100% reduction in T1-Gd enhancing lesions; 10.6% mean decrease in T2 lesion volume; 93% of subjects relapse free, and an annualized relapse rate (ARR) of 0.07. Ublituximab was well tolerated; the most common adverse events was infusion related reactions (all grade 1-2). No discontinuations due to AEs were reported. Ublituximab continues to be well tolerated, with a median duration of follow-up of 124.7 weeks, no drug related discontinuations and only one AE deemed at least possibly related to ublituximab that occurred in more than 1 patient, which was infusion related reaction (IRR) all grade 1 or 2 in severity. At the time of presentation, long-term safety information will be presented for all patients on the OLE.

Conclusions: The Phase 2 OLE data support that ublituximab continues to be safe, well tolerated and effective with one-hour infusions. These results support the ongoing Phase 3 ULTIMATE program in RMS.

Disclosure: *Edward J. Fox: Biogen, Celgene, Chugai, EMD Serono, MedDay (consulting fee). Genentech/Roche, Sanofi/Genzyme, Teva (speakers bureau). Edward J. Fox, Amy Lovett-Racke: Novartis, TG Therapeutics (contracted research). Sibyl Wray: Biogen, EMD Serono, Genentech/Roche (speakers bureau). Genzyme/Sanofi, Hope Neurology (consulting fee). Richard Shubin: Nothing to disclose. Deren Huang: Biogen, Novartis (consulting fee, speakers bureau). Celgene, Genentech (consulting fee). Teva (speakers bureau). Ann D. Bass: Actelion, Genentech-Roche, TG Therapeutics (contracted research). Biogen, EMD Serono, Novartis (speakers bureau). Mallinkrodt, Sanofi-Genzyme (consulting fee). Michael S. Weiss, Sean Power, Jenna Bosco, Koby Mok: TG Therapeutics (salary).*

Keywords: Disease-modifying treatments in MS

(DXT18)

Adherence and Compliance with Subcutaneous Administration of Ofatumumab in Relapsing Multiple Sclerosis

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Background: Ofatumumab (OMB), the first fully human anti-CD20 monoclonal antibody, administered with a monthly 20 mg subcutaneous (s.c.) dosing regimen, demonstrated superior efficacy versus teriflunomide (TER) in the two Phase 3 ASCLEPIOS I and ASCLEPIOS II trials in relapsing multiple sclerosis. Patients who completed the double-blind phase of the trials on study drug were eligible for transition to the ongoing open-label extension study ALITHIOS.

Objectives: To evaluate treatment discontinuation and compliance with OMB and TER treatment in the Phase 3 ASCLEPIOS I/II trials and to assess patients' acceptance of transitioning to the ALITHIOS study.

Methods: In ASCLEPIOS I/II, patients were randomized (1:1) to OMB 20 mg s.c. (loading doses, administered at clinic: Days 1, 7, and 14; maintenance doses, administered at home: every 4 weeks from Week 4) or TER 14 mg (orally once daily), for up to 30 study months. Here we report on treatment discontinuation and compliance (defined as exposure to study drug [days]/on-treatment period [days]×100%) in ASCLEPIOS trials and percentage of eligible ASCLEPIOS patients who accepted to transition to the ALITHIOS study and the compliance in this study.

Results: In ASCLEPIOS I, 759/927 (81.9%) randomized patients (OMB: 400/465 [86.0%]; TER: 359/462 [77.7%]) completed the study on study drug. The proportion of patients discontinuing treatment were OMB, 14.0%; TER, 21.2%. The most common reasons for discontinuation (>2% in any group) were patient/guardian decision (OMB: 4.9%; TER: 8.2%), adverse event (OMB: 5.2%; TER: 5.0%), and physician decision (OMB: 2.2%; TER: 6.5%). In ASCLEPIOS II, 753/955 (78.8%) randomized patients (OMB: 383/481 [79.6%]; TER: 370/474 [78.1%]) completed the study on study drug. Proportion of patients discontinuing treatment were OMB, 20%; TER, 21.5%; reasons for discontinuation were patient/guardian decision (OMB: 7.3%; TER: 7.8%), adverse event (OMB: 5.6%; TER: 4.9%) and physician decision (OMB: 5.2%; TER: 6.8%). In both trials compliance was high (>95% of patients falling in the ≥90% compliance category) across treatment groups. Approximately 90% of eligible patients consented to participate in the open-label study; compliance data will be presented.

Conclusions: In ASCLEPIOS trials compliance with home-administered s.c. OMB was high and fewer patients discontinued OMB as compared to TER. The majority of eligible patients accepted transition to the open-label ALITHIOS extension study.

Disclosure: *Edward Fox: Biogen, Celgene, Chugai, EMD Serono, Genentech/Roche, MedDay, Novartis, Sanofi, Genzyme, Teva, TG Therapeutics (advisory work, consulting fee, contracted research, speakers bureau). Lori*

Mayer: Biogen, Novartis, Celgene, Genentech, EMDSereno (consulting fee, speakers bureau). Angela Aungst: Nothing to disclose. Alexandra Goodyear, Cecile Kerloeguen: Novartis (salary). Linda Mancione: Novartis Pharmaceuticals Corporation (salary). Nicola Rennie, Dee Stoneman, Martin Zalesak, Marina Ziehn: Novartis Pharma AG (salary). Derrick Robertson: Biogen, Celgene, EMD Serono, Genentech, Novartis, Sanofi Genzyme, Teva, (consulting fee). Biogen, Celgene, EMD Serono, Genentech, Novartis, Sanofi Genzyme, Teva, Actelion, Mallinckrodt, MedDay, PCORI, TG Therapeutics (contracted research). Biogen, Celgene, EMD Serono, Genentech, Novartis, Sanofi Genzyme, Teva, Mallinckrodt, Acorda (speakers bureau). Jeffrey A. Cohen: Adamas, Convelo, Mylan, Population Council (consulting fee). Multiple Sclerosis Journal (co-editor).

Keywords: Compliance , Disease-modifying treatments in MS

(DXT20)

Glatiramer Acetate (GA) Produced By Mapi Pharma Is Equivalent to Commercially Available GA Preparations

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Background: Glatiramer Acetate (GA) is one of the first disease modifying treatments approved for relapsing-remitting multiple sclerosis. Recently, several generic equivalents of GA were approved for marketing in the USA. Mapi is developing GA to be used in Glatiramer Acetate Depot (GA Depot) and in Mapi's generic GA. Here, we present key characteristic data from physicochemical (structural) and biological (pharmacodynamic) assays that were conducted to compare Mapi's GA and all US-approved GA equivalents.

Objectives: To demonstrate through the results (physicochemical and biological) that Mapi's GA is similar to US-approved and commercially available GA equivalents.

Methods: Mapi's GA is produced using the same starting materials and basic chemistry as Copaxone®. At least five batches of Copaxone®, one batch of Glatopa™ (Sandoz), one batch of Glatiramer Acetate Injection (Mylan) and several batches of Mapi's GA were analyzed for physicochemical properties (molecular weight distribution, impurities profile, amino-acid composition and spectral fingerprint) and various structural signatures. A representative batch of Mapi's GA was compared with three different commercially available GA preparations using a bioassay test (MOG-induced EAE in mice).

Results: The selected tests and data presented here represent a portion of a broader set of physicochemical and biological assays that were conducted. No differences were observed in the physicochemical properties or the structural signatures between Mapi's GA and all other US-approved GA equivalents. Equivalent pharmacodynamic activity of Mapi's GA to three commercially available GA preparations (Copaxone®, Glatopa™ and Glatiramer Acetate Injection) was demonstrated using MOG-induced EAE in mice.

Conclusions: Mapi's GA is equivalent to commercially available GA products in physicochemical properties, structural signatures and biological activity as demonstrated by bioassay and complies with the FDA's guidance for generic GA. These results will support GA Depot and a new generic GA version commercialization by Mapi Pharma.

Disclosure: *Susanna Tchilibon, Nadav Bleich Kimelman, Shai Rubnov, Laura Popper, Uri Danon: Mapi Pharma Ltd. (employer/employee relationship). Ehud Marom: Mapi Pharma Ltd. (salary).*

Keywords: Disease-modifying treatments in MS

(DXT22)

Characterization of Incidence and Time-to-Recovery from Grade 3/4 Lymphopenia Lasting >=6 Months in Patients with Multiple Sclerosis Treated with Cladribine Tablets

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Background: Patients with multiple sclerosis (MS) treated with cladribine tablets (CT) are expected to experience lymphopenia because of its mechanism of action (MOA), and transient mild-to-moderate lymphopenia has been observed in the majority of patients. Given that a reduction in overall lymphocyte counts is part of the MOA of cladribine, further studies on the severity of lymphopenia are warranted.

Objectives: To examine the effect of CT 3.5 mg/kg (CT3.5, cumulative over 2 years) on Grade 3/4 lymphopenia lasting ≥6 continuous months post-baseline in subjects with baseline absolute lymphocyte count (ALC) within normal limits from the CT3.5 monotherapy oral cohort, defined as the safety populations of the Phase 3 CLARITY, CLARITY Extension, and ORACLE-MS studies of MS, and long-term follow-up in the PREMIERE registry.

Methods: In this *post hoc* analysis, combined data from 2 years of Phase 3 studies and the follow-up PREMIERE registry were analyzed on the incidence of Grade 3/4 lymphopenia (ALC <500/mm^3) lasting ≥6 months. Time to an episode and time to recovery were also assessed. Recovery from Grade 3/4 lymphopenia is defined as a return to Grade ≤2 lymphopenia.

Results: Of the 923 patients randomized to CT3.5, 891 (96.5%) had baseline ALC within normal limits (Grade 0), and in this subpopulation, 218 (23.6%) experienced at least a single reading of

Grade 3/4 lymphopenia, and 33 (3.6%) experienced Grade 3/4 lymphopenia lasting ≥6 months (38 episodes). More patients with Grade 3/4 lymphopenia lasting ≥6 months were female (81.8% vs. 66.1%), had used ≥1 prior disease-modifying drug (33.3% vs. 19.5%), and had more severe disease (≥9 T2 lesions [93.9% vs. 88.1%], ≥1 relapse [75.8% vs. 53.9%], higher median score on Expanded Disability Status Scale [3.0 vs. 2.0]) at baseline versus the overall patients with baseline ALC within normal limits. Of the 33 CT3.5-treated patients with Grade 3/4 lymphopenia lasting ≥6 months, more experienced the episode in Year 2 than in Year 1 of the core studies (64% vs. 18%), with a median (Q1, Q3) time to first episode of 58.9 (51.1, 83.1) weeks. Of the 38 Grade 3/4 lymphopenia (≥6 months) episodes, 27 (71.1%) lasted 24–48 weeks, and 11 (28.9%) lasted >48 weeks. Median (Q1, Q3) time to recovery from first Grade 3/4 lymphopenia (≥6 months) episode was 36.3 (28.4, 66.3) weeks.

Conclusions: The incidence of Grade 3/4 lymphopenia lasting ≥6 months in patients treated with CT3.5 was low. Most episodes (71.1%) of Grade 3/4 lymphopenia lasting ≥6 months resolved within 6 months to 1 year.

Disclosure: *Gabriel Pardo: Abbvie, Adamas, Alkermes, Sanofi Genzyme, Teva (research support). Alexion, Celgene, Sanofi-Genzyme (consulting fee). Biogen Idec, EMD Serono, Novartis, Roche/Genentech (consulting fee, research support). Kottil Rammohan: Abbvie, Adamas, Alkermes, Roche/Genentech, Sanofi Genzyme, Teva (research support to the institution). Alexion, Celgene, Roche/Genetech, Sanofi-Genzyme (consulting fee). Biogen Idec, EMD Serono, Novartis (consulting fee, research support to the institution). Thomas P. Leist: Acorda, Biogen Idec, EMD Serono, Genzyme, Novartis, Roche/Genentech, Sanofi-Aventis, Teva Neurosciences (speakers bureau). Julie Aldridge, Matt Mandel, Daniel Jones: EMD Serono, Inc. (a business of Merck KGaA, Darmstadt, Germany) (salary). Ciara Rossier, Andrew Galazka: Merck KGaA, Aubonne, Switzerland (a business of Merck KGaA, Darmstadt, Germany) (salary). Axel Nolting: Merck KGaA (salary). Gavin Giovannoni: Abbvie, Actelion, Almirall, Atara Bio, Bayer Schering Pharma, FivePrime, GlaxoSmithKline, GW Pharma, Merck KGaA, Pfizer Inc, Protein Discovery Laboratories, Sanofi-Genzyme, Teva Pharmaceuticals Industries Ltd, UCB, Vertex Pharmaceuticals (consulting fee). Biogen Idec, Ironwood, Merck and Co, Novartis (consulting fee, unrelated research support).*

Keywords: Disease-modifying treatments in MS, Immunology and MS

(DXT23)

Disease-Modifying Therapy Landscape: An Evaluation of Cost and Care

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Background: Multiple sclerosis (MS) affects ~1 million people in the US and is the fourth largest specialty drug spend. Over the years many disease-modifying therapies (DMT) have come to market, resulting in increased drug choice and spend. Patient's often struggle with the cost and chronicity of these therapies.

Objectives: Evaluate DMT utilization, cost, adherence and switching in a commercial MS population.

Methods: We analyzed DMT use data of 34.2 million beneficiaries with a pharmacy benefit plan administered by a large pharmacy benefit manager for the two-year period 2017-2018. Unit cost trend is defined as the rate of cost change due to inflation, discounts, drug mix and member cost and is determined on a per-member-per-year (PMPY) basis. Adherent patients were defined as an average medication possession ratio (MPR) of ≥80%. Switching occurred when an alternative DMT claim occurred after the index DMT drug claim.

Results: DMT prevalence was 0.09% in 2018. PMPY spend for DMT to treat MS decreased 4.8% in 2018, driven by a 7.8% utilization decrease. Utilization trend was negative year over year. Branded medications Tecfidera® (dimethyl fumarate), Gilenya® (fingolimod) and Avonex® (interferon beta-1a) account for more than 44% of DMT prescribed in this class and each of these increased in unit cost (range 3.7- 6.0%). Utilization of Copaxone® (glatiramer acetate) declined by 59.6%, influenced by generic availability. Generic DMT fill rate rose from 5.2 to 17.0% in year over year.

In 2018, just over 27% of patients utilizing MS medications were non-adherent to their DMT. This represents a 1.4% year over year improvement in adherence. Nearly 15% of patients initiating a DMT switched to another medication within one year of the initial prescription.

Utilization declined for injected interferons, such as Avonex, Rebif® (interferon beta-1a) and Betaseron® (interferon beta-1b), as market share shifts to oral medications such as Aubagio® (teriflunomide), which had a 4.2% utilization increase in 2018. Not all new therapies are oral. Some of the newer DMT options are infrequently administered infused (IV) products, such as Ocrevus® (ocrelizumab). Claims for IV DMT may adjudicate through the medical benefit and not be fully appreciated in this analysis.

Conclusions: Knowledge of DMT trends can assist in reducing costs and identifying opportunities for further study. A significant portion of MS patients struggle with adherence. Early identification of non-adherent patients and application of customized support may help optimize therapeutic outcomes.

Disclosure: *Gail Bridges, Douglas Mager, Mary Dorholt, Rochelle Henderson: Express Scripts (salary).*

Keywords: Adherence, Disease-modifying treatments in MS, Economic issues and MS

(DXT24)

Two Expanded Disability Status Scale Subscales Evaluated in Patients with Relapsing-Remitting or Secondary Progressive Multiple Sclerosis

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Background: In phase 3 trials using the Expanded Disability Status Scale (EDSS), fingolimod and siponimod reduced disability worsening in patients with relapsing-remitting multiple sclerosis (RRMS) and secondary progressive MS (SPMS), respectively. However, EDSS components may differentially contribute to worsening, and contribution of each component may depend on disease stage. Also, EDSS assessments can be burdensome for patients and clinicians. Using factor analysis, different EDSS functions can be allocated to two novel subscales, including parameters most relevant to disease worsening.

Objectives: Evaluate the effects of fingolimod and siponimod using EDSS subscales derived by factor analysis of phase 3 trial data.

Methods: PROC FACTOR procedure was used to determine best fit of baseline EDSS data to the following subscales: Motor Integration (MI: ambulation, cerebellar and pyramidal functions) and Collateral (C: bowel and bladder, brainstem, cerebral, sensory and visual functions). Treatment effect sizes (ES) on disability (mean change from baseline vs placebo) were determined overall and by each subscale up to 24 months (M) in RRMS patients from FREEDOMS and up to 27M in SPMS patients from EXPAND. Statistical significance was assessed using rank analysis of covariance (FREEDOMS) and a covariance mixed-effect, repeat-measurement model (EXPAND). Subgroup analyses of patients in EXPAND with/without lesion activity or relapses prior to screening were also performed and will be presented. Analyses were for hypothesis generation without multiple comparison adjustment.

Results: Treatment ES in FREEDOMS (N=843: fingolimod, n=425; placebo, n=418) at 24 months were −0.14, p=0.002 (EDSS); −0.18, p=0.002 (MI); −0.07, p=0.081 (C). Significant effects ($p<0.05$) were seen on MI from M6; effects on C were mostly nonsignificant. In EXPAND (N=1645: siponimod, n=1099; placebo, n=546), overall treatment effects were detected over 27M for EDSS (p=0.020), MI (p=0.014) and C (p=0.021). Significant ES were seen on MI (all $p<0.01$) at M9 (−0.28), 15 (−0.34) and 18 (−0.34), and on C at M18 (−0.24, $p<0.05$) and 27 (−0.54, $p<0.001$).

Conclusions: The benefits of fingolimod in patients with RRMS mainly impacted the MI subscale. For patients with SPMS, the benefits of siponimod were seen on both MI and C. In SPMS, effects on MI appeared earlier than on C, however the largest ES was seen later on C. Defining EDSS subscales with factor analyses may help improve their clinical usefulness.

Disclosure: *Gary Cutter: Avexis Pharmaceuticals, Biolinerx, Brainstorm Cell Therapeutics, CSL Behring, Galmed Pharmaceuticals, Hisun Pharmaceuticals, Horizon Pharmaceuticals, Merck, Merck/Pfizer, Neurim, NHLBI (Protocol Review Committee), NICHD (OPRU oversight committee), Ophazyme, Opko Biologics, Reata Pharmaceuticals, Receptos/Celgene, Sanofi-Aventis, Teva Pharmaceuticals, Vivus (data and safety monitoring boards). Biogen, Click Therapeutics, Genentech, Genzyme, Gilgamesh Pharmaceuticals, GW Pharmaceuticals, Klein-Buendel Incorporated, MedDay, MedImmune, Osmotica Pharmaceuticals, Perception Neurosciences, Recursion Pharmaceuticals, Roche, Somahlution, TG Therapeutics (consulting fee). Novartis (consulting fee, data and safety monitoring boards). Pythagoras, Inc. (president). University of Alabama at Birmingham (salary). Xiangyi Meng, Jamie L. Weiss, Wendy Su: Novartis Pharmaceuticals Corporation (salary). Ralph H B Benedict: Acorda, Mallinckrodt, NIH, NMSS (contracted research). Biogen (cme speaker fees , consulting fee, contracted research). Celgene, EMD Serono (cme speaker fees , consulting fee). Genentech, Genzyme, Novartis (consulting fee, contracted research). Psychological Assessment Resources, Inc. (royalty). Roche, Sanofi, Takeda, Verasci (consulting fee). Stanley L. Cohan: AbbVie, Adamas, Alexion, MedDay, Sage Bionetworks (contracted research). Biogen, Novartis, Sanofi Genzyme (consulting fee, contracted research, speakers bureau). EMD Serono, Pear Therapeutics (consulting fee). Genentech, Roche (contracted research, speakers bureau). Bruce A C Cree: Akili, Alexion, Atara, Biogen, EMD Serono, Novartis, TG Therapeutics (consulting fee). Florian P. Thomas: Biogen, Teva Neuroscience (contracted research). Genentech, Novartis, Sanofi Genzyme (consulting fee).*

Keywords: Disease-modifying treatments in MS

(DXT26)

Long-Term Disease Stability Assessed By the Expanded Disability Status Scale in Patients Treated with Cladribine Tablets in the Clarity and Clarity Extension Studies

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Background:
Treatment with cladribine tablets 10mg (cumulative dose 3.5 mg/kg [CT3.5] over 2 years) in CLARITY and CLARITY Extension reduced relapse rate and slowed disability progression versus placebo in patients with relapsing-remitting multiple sclerosis (RRMS)

Objectives:
The objective of this *post hoc* analysis was to evaluate long-term disease stability assessed by the Expanded Disability Status Scale (EDSS) after treatment with CT3.5 in patients with RRMS enrolled in CLARITY and CLARITY Extension

Methods:
Patients randomized to CT3.5 in CLARITY and then randomized to placebo in CLARITY Extension, with at least 1 post-baseline EDSS measurement, were included (CP3.5; n=98). This analysis assessed EDSS score over time (from CLARITY randomization to end of follow-up in CLARITY Extension, including the bridging interval between studies) at 6-monthly intervals, and separately time to 3- and 6-month confirmed EDSS score progression from CLARITY baseline. EDSS score worsening or improvement in each year was defined as any increase or decrease, respectively, in minimum EDSS score at 6-monthly intervals; all other cases were classified as stable. An increase or decrease was defined as an EDSS score change of 1.5 points (baseline EDSS 0), 1 point (baseline EDSS ≤4.5), or 0.5 point (baseline EDSS ≥5.0).

Results:
Five years after CLARITY baseline, median EDSS remained stable compared with baseline values. Median EDSS score (95% confidence interval [CI]) for patients in the CP3.5 group was 2.5 (2.0–3.5) compared with 3.0 (2.5–3.5) at baseline. In each 12-month period, EDSS score stability was observed in >50% of patients, improvement in 21–30% of patients, and worsening in 0–25%. During Year 5 in the CP3.5 group, EDSS stability was observed in 53.9% of patients, improvement in 21.3%, and worsening in 24.7%. Less than 30% of patients reached 3- or 6-month confirmed EDSS progression by Year 5.

Conclusions:
EDSS score was stable up to 5 years post-CLARITY baseline for the CP3.5 group. Between 20–30% of patients demonstrated improvement in EDSS score versus baseline each year.

Disclosure: *Gavin Giovannoni: Abbvie, Actelion, Almirall, Atara Bio, Bayer Schering Pharma, FivePrime, GlaxoSmithKline, GW Pharma, Merck KGaA, Pfizer Inc, Protein Discovery Laboratories, Sanofi-Genzyme, Teva Pharmaceuticals Industries Ltd, UCB, Vertex Pharmaceuticals (consulting fee). Biogen Idec, Ironwood, Merck and Co, Novartis (consulting fee, unrelated research support). Giancarlo Comi: Almirall SpA, Biogen Idec, Biogen Italia Srl, Celgene Group, Excemed, F. Hoffman-La Roche, Forward Pharma, Genzyme Corporation, Genzyme Europe, Medday, Merck KGaA, Merck Serono SpA, Novartis, Roche SpA, Sanofi Genzyme, Teva Italia Srl, Teva Pharmaceutical Industries Ltd. (consulting fee). Kottil Rammohan: Acorda, Biogen Idec, EMD Serono, Genzyme, Novartis, Roche/Genentech, Sanofi-Aventis, Teva Neurosciences (speakers bureau). Peter Rieckmann: Bayer Shering Pharma, Biogen Idec, Boehringer-Ingelheim, Genzyme, Merck, Novartis, Sanofi-Aventis, Serono Symposia International Foundation, Teva Pharmaceutical Industries (speakers bureau). Patrick Vermersch: Almirall, Celgene, Novartis, Roche (consulting fee). Bayer, Biogen, Merck KGaA, Sanofi-Genzyme (consulting fee, research support). Fernando Dangond: EMD Serono, Inc. (a business of Merck KGaA, Darmstadt, Germany) (salary). Birgit Keller, Dominic Jack: Merck KGaA (salary).*

Keywords: Disease-modifying treatments in MS

(DXT27)

Integrated Lymphopenia Analysis in Younger and Older Patients with Multiple Sclerosis Treated with Cladribine Tablets

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Background:
The mechanism of action of cladribine is thought to be related to a reduction in lymphocyte counts. As the immune system undergoes changes with aging, it is not currently well understood whether the impact of cladribine tablets (CT) on lymphocyte counts differs in younger versus older patients.

Objectives:
To examine the effect of age (≤50 and >50 years [yr]) at baseline and after treatment with placebo (PBO) or CT 3.5 mg/kg (CT3.5, cumulative over 2 yrs) on lymphopenia in patients enrolled in the Phase 3 CLARITY, CLARITY Extension, and ORACLE-MS studies, and long-term follow-up in the PREMIERE registry.

Methods:
In this *post hoc* analysis, combined data from two yrs of Phase 3 studies on levels of absolute lymphocyte count (ALC), incidence of Grade 3/4 lymphopenia, and time to recovery from severe lymphopenia were analyzed in patients by baseline age group.

Results:
This analysis was carried out in 1564 patients: age ≤50: PBO N=566, CT3.5 N=813; age >50: PBO N=75, CT3.5 N=110. In both age groups, CT3.5 treatment resulted in a 43.1–47.6% reduction in mean ALC versus PBO at Week (wk) 9, which was after completing the Yr 1 doses. Mean (standard deviation [SD]) ALC in the CT3.5 groups at Wk 9 were: age ≤50: 1.12 (0.50) $x10^9$/L; age >50: 1.00 (0.42) $x10^9$/L. ALC levels in the CT3.5-treated groups gradually increased thereafter up to Wk 48 (mean [SD] ALC at Wk 48: age ≤50: 1.27 [0.45] $x10^9$/L; age >50: 1.32 [0.51] $x10^9$/L); ALC remained 34.5–35.6% below those treated with PBO. In Yr 2 at Wk 55, CT3.5 treatment resulted in a 54.6–60.8% reduction in mean ALC versus PBO (Yr 2 doses completed). Mean (SD) ALC in the CT3.5 groups at Wk 55 were: age ≤50: 0.89 (0.39) $x10^9$/L; age >50: 0.80 (0.33) $x10^9$/L. ALC levels in the CT3.5-treated groups gradually increased thereafter up to Wk 96 (mean [SD] ALC at Wk 96: age ≤50: 1.11 [0.42] $x10^9$/L; age >50: 1.11 [0.37] $x10^9$/L); ALC remained 42.8–43.7% below those treated with PBO. Incidence of Grade 3/4 lymphopenia was higher with CT3.5 versus PBO in Yr 1 (age ≤50: 8.3%; age >50: 10.0%; vs. 0–0.4% in PBO) and Yr 2 (age ≤50: 18.7%; age >50: 20.0%; vs. 0–0.2% in PBO). Median time to recovery from Grade 3/4 to ≤2 lymphopenia was 1.18 and 1.54 months for CT3.5-treated patients in the age ≤50 and >50 groups, respectively.

Conclusions:
ALC changes in CT3.5-treated patients were similar in older and younger patients relative to PBO-treated patients during two yrs of active treatment as expected. Recovery time from lymphopenia was also similar between the age groups.

Disclosure: *Gavin Giovannoni: Abbvie, Actelion, Almirall, Atara Bio, Bayer Schering Pharma, FivePrime, GlaxoSmithKline, GW Pharma, Merck KGaA, Pfizer Inc, Protein Discovery Laboratories, Sanofi-Genzyme, Teva Pharmaceuticals Industries Ltd, UCB, Vertex Pharmaceuticals (consulting fee). Biogen Idec, Ironwood, Merck and Co, Novartis (consulting fee, unrelated research support). Patricia K. Coyle: Accordant, Acorda Therapeutics, Bayer HealthCare, Biogen, Celgene, EMD serono, Genzyme/Sanofi, Teva Pharmaceuticals USA (consulting fee). Actelion, Alkermes, MedDay, NINDS (contracted research). Genentech/Roche, Novartis (consulting fee, contracted research). Patrick Vermersch: Almirall, Celgene, Novartis, Roche (consulting fee). Biogen, Merck KGaA, Sanofi-Genzyme, Teva (consulting fee, research support). Bryan Walker: Biogen, Celgene, EMD Serono, Novartis, Sanofi-Genzyme (consulting fee). Julie Aldridge, Sana Syed, Daniel Jones: EMD Serono, Inc. (a business of Merck KGaA, Darmstadt, Germany) (salary). Axel Nolting: Merck KGaA (salary). Andrew Galazka: Merck KGaA, Aubonne, Switzerland (a business of Merck KGaA, Darmstadt, Germany) (salary). Thomas P. Leist: Alkermes, Bayer, Biogen, EMD Serono, Genentech, Genzyme, Novartis (consulting fee).*

Keywords: Disease-modifying treatments in MS, Immunology and MS

(DXT28)

Effectiveness of Cladribine Tablets in Patients with Relapsing-Remitting Multiple Sclerosis with Baseline EDSS >=3.5 or =<3.0 in Clarity

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Background:
In the Phase 3 CLARITY study, patients with relapsing-remitting multiple sclerosis (MS) treated with cladribine tablets (CT) 10 mg (3.5 mg/kg [CT3.5] or 5.25 mg/kg cumulative dose over two years), showed significant reductions in annualized relapse rate (ARR, $P<0.001$), time to 3-month (mo) sustained change in Expanded Disability Status Scale (EDSS, $P\leq0.03$), and lesion activity on brain magnetic resonance imaging (MRI, all $P<0.001$) vs placebo (PBO). However, the efficacy of CT has not been fully characterized in patients transitioning to active secondary progressive MS or not, for which EDSS scores of ≥3.5 and ≤3.0, respectively, can be used as a proxy definition.

Objectives:
To examine differences between PBO and CT3.5 on clinical and MRI endpoints and in attainment of No Evidence of Disease Activity (NEDA) in patients with baseline EDSS scores of ≥3.5 or ≤3.0 in CLARITY.

Methods:
In this post-hoc analysis, Week 96 data from CLARITY were retrospectively examined across patients with baseline EDSS ≥3.5 or ≤3.0 for relapses, 3- or 6-mo confirmed disability progression (CDP, per EDSS score changes), new T1 gadolinium-enhancing (Gd+) lesions, active T2 lesions, and NEDA.

Results:
Baseline characteristics were evenly distributed across treatment groups. Relapse, T1 Gd+ lesion, and T2 lesion numbers were greater in PBO-treated vs CT3.5-treated patients for both baseline EDSS groups (all P<0.0001, nominal significance) at Week 96. For patients with baseline EDSS ≥3.5, CT3.5 treatment resulted in improvements in qualifying relapses (Kaplan-Meier estimates at last event: 78.3% vs 60.3%), 3-mo CDP (83.5% vs 69.4%), and 6-mo CDP (88.1% vs 78.2%) vs PBO. Differences between CT3.5 and PBO treatment in the baseline EDSS ≤3.0 group were: 81.1% vs 61.6% in qualifying relapse, 86.3% vs 80.6% in 3-mo CDP, and 92.0% vs 87.2% in 6-mo CDP. Odds ratios (OR) favored CT3.5 vs PBO for NEDA based on either 3-mo (OR: 4.40) and 6-mo CDP (OR: 4.11) in the baseline EDSS ≥3.5 group and in the baseline EDSS ≤3.0 group (OR for 3-mo CDP: 4.23; OR for 6-mo CDP: 4.62; all P<0.0001, nominal significance).

Conclusions:
Cladribine tablets treatment resulted in similar improvements in relapse and MRI outcomes regardless of patient baseline EDSS score. The effect of cladribine tablets on NEDA composites was also favorable across patients with baseline EDSS ≥3.5 or ≤3.0.

Disclosure: *Giancarlo Comi: Almirall SpA, Biogen Idec, Biogen Italia Srl, Celgene Group, Excemed, F. Hoffman-La Roche, Forward Pharma, Genzyme Corporation, Genzyme Europe, Medday, Merck KGaA, Merck Serono SpA, Novartis, Roche SpA, Sanofi Genzyme, Teva Italia Srl, Teva Pharmaceutical Industries Ltd. (consulting fee). Gabriel Pardo: Abbvie, Adamas, Alkermes, Sanofi Genzyme, Teva (research support). Alexion, Celgene, Sanofi-Genzyme (consulting fee). Biogen Idec, EMD Serono, Novartis, Roche/Genentech (consulting fee, research support). Fernando Dangond, Julie Aldridge, Caroline Lemieux: EMD Serono, Inc. (a business of Merck KGaA, Darmstadt, Germany) (salary). Kottil Rammohan: Acorda, Biogen, EMD Serono, Genzyme, Novartis, Roche/Genentech, Sanofi-Aventis, Teva Neurosciences (speakers bureau).*

Keywords: Disease-modifying treatments in MS

(DXT29)

Acapella: Real-World Experience with Ocrelizumab: An Observational Study Evaluating Safety in Patients with Relapsing and Progressive MS, Year Three Data

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Background: Ocrelizumab (OCR) is a humanized, monoclonal antibody targeting CD20+ B-cells and is approved for the treatment of relapsing remitting (RRMS) and primary progressive MS (PPMS). The ACAPELLA trial is a prospective study with a primary objective of assessing OCR-associated adverse events (AEs) in a real-world MS population. ACAPELLA includes patients with preexisting conditions exempted from the phase II & III clinical trials, such as a prior history of malignancy, prior immunosuppressive treatment, and more advanced age and/or disability. Interim data analyses occur on a biannual basis and findings are reported yearly. This is the third iteration.

Objectives: We sought to determine the frequency of serious infections and malignancy in a real-world population receiving OCR with characteristics outside the inclusion parameters of the phase II and III trials.

Methods: The study includes all subjects treated with OCR at the Elliot Lewis Center since its commercial release in March 2017. Initial assessments include EDSS, brain MRI, mammograms (standard of care), collection of medical history including prior serious or recurrent infections, history of malignancy and exposure to immunosuppressive treatment, JCV index, and CD19 count.

Results: As of December 2019, 291 subjects were enrolled, 181 subjects had reached 12 months of treatment, 131 subjects had reached 18 months, and 84 subjects had reached 24 months. Subjects were 29% male, 71% female, with an age range of 18-73. Sixty three percent had RRMS and 37% PMS (PPMS and progressive RRMS) with an EDSS range of 0-7.5; 25% had a baseline EDSS of $\geq$ 6.0 with a median of 3.0.

The rate of infections for all OCR-treated patients was 43% (6% bronchitis, 2% shingles, 56% URIs, 30% UTIs, 4% HSV, and 25% other infections. Four percent of subjects had a serious infection (one that required hospitalization, was felt to be life-threatening, or resulted in death). Three percent of subjects had clinical or MRI relapses. 8% of subjects had a history of prior neoplasm (excluding basal cell carcinoma). Two malignancies have occurred during OCR treatment.

Conclusions: Thus far, the incidence of AEs is comparable to that seen in the phase III trials and in previously reported ACAPELLA data. Additional topics of interest in the ACAPELLA population include the effect of continued OCR dosing on JCV index values and immunoglobulin levels, and changes in EDSS and MRI over time.

Disclosure: *Nothing to disclose.*

Keywords: Disease-modifying treatments in MS, Ocrelizumab

(DXT30)

Acapella: Hypogammaglobulinemia and JCV Status in Ocrelizumab-Treated Patients, Year Two Data

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Background: Ocrelizumab (OCR) is a humanized anti-CD20 monoclonal antibody approved for the treatment of relapsing remitting (RRMS) and primary progressive multiple sclerosis (PPMS). Immunoglobulin levels were monitored during the phase III trials, and 1.5% of patients developed low immunoglobulin G (IgG) values after 2-3 years of OCR treatment, potentially increasing the risk of infections. The JCV antibody index used to stratify PML risk in patients treated with natalizumab was not studied and the impact of long-term B-cell suppression on JCV and IgG titers is unknown.

Objectives: As part of the ACAPELLA trial, a prospective study with a primary objective of assessing OCR-associated adverse events (AEs) in a real-world MS population, we sought to evaluate the impact of OCR treatment on immunoglobulin levels and JCV titers over time.

Methods: The study includes all subjects receiving OCR at the Elliot Lewis Center followed prospectively since March 2017. Subjects are monitored for the occurrence of infections and other serious adverse events (SAEs) and have biannual assessments of serum immunoglobulin levels and JCV antibody titers.

Results: As of December 2019, 291 patients have been treated with OCR and enrolled in ACAPELLA: 181 have been treated for at least 12 months, 131 have been treated for at least 18 months, and 84 subjects have reached 24 months. Two hundred eighty-one of the total 291 subjects had IgG levels drawn at baseline. Twenty-seven subjects (10%) had IgG levels below the lower limit of normal (LLN) at baseline. Of the 27 patients with low IgG at baseline, 19 have received treatment for at least 12 months. Of those 19, 4 patients were seen to have a >10% drop in IgG level after 12 months. Ten patients developed at least one low IgG level after 12-24 months of treatment exposure, although many returned to normal.

Two hundred eighty-one of the total 291 patients had a baseline JCV index. Ninety-three (33%) had titers <0.4, 73 (26%) between 0.4-1.5, and 115 (41%) >1.5. In our two-year data, three patients had a change in JCV status from positive to negative between 12 and 24 months of treatment duration. Year three data is characterized n the poster.

Conclusions: The frequency of persistent hypogammaglobulinemia was low in this cohort of patients and thus far has not been associated with an increased risk of infection. Three patients had a change in JCV status from positive to negative, and the effect of JCV index in the remaining subjects is further characterized.

Disclosure: *Nothing to disclose.*

Keywords: Disease-modifying treatments in MS, Immunology and MS, Ocrelizumab

(DXT31)

Impact of Eculizumab on Hospitalization Rates and Relapse Treatment in Patients with Neuromyelitis Optica Spectrum Disorder: Phase 3 Prevent Study

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Background: Relapses resulting in hospitalization are common in patients with the rare autoimmune inflammatory disease neuromyelitis optica spectrum disorder (NMOSD). The randomized, double-blind, placebo-controlled PREVENT study (NCT01892345) assessed the safety and efficacy of eculizumab in aquaporin-4 immunoglobulin G (AQP4-IgG)-positive NMOSD. Eculizumab significantly reduced the risk of adjudicated relapse compared with placebo (primary endpoint).

Objectives: To evaluate rates of relapse-related hospitalization and associated treatment in patients with AQP4-IgG-positive NMOSD receiving eculizumab versus placebo in the PREVENT study.

Methods: Patients with AQP4-IgG-positive NMOSD were randomized 2:1 to receive eculizumab (maintenance dose, 1200 mg/2 weeks, n = 96) or placebo (n = 47) with/without stable-dose concomitant immunosuppressant therapy (excluding rituximab and mitoxantrone). Hospitalizations were recorded as a component of the adverse-event tracking performed throughout the study. The annualized relapse-related hospitalization and treatment rates were defined as the total number of relapses requiring hospitalization, and associated acute treatments, respectively, divided by the total number of patient-years in the study period.

Results: The median exposure to treatment was 89.43 weeks for eculizumab and 41.29 weeks for placebo. The overall annualized hospitalization rate was 0.26 and 0.78 ($p < 0.0001$) in the eculizumab and placebo groups, respectively. The annualized relapse-related hospitalization rate was significantly lower in the eculizumab group than in the placebo group: 0.04 versus 0.31, respectively ($p < 0.0001$). The annualized relapse-related use of intravenous methylprednisolone, plasma exchange and high-dose oral corticosteroids for eculizumab versus placebo was 0.07 versus 0.42 ($p < 0.0001$), 0.02 versus 0.19 ($p = 0.0001$) and 0.04 versus 0.11 ($p = 0.0733$), respectively.

Conclusions: Treatment with eculizumab significantly reduced relapse-related hospitalizations and their associated treatment rates in patients with AQP4-IgG-positive NMOSD versus placebo, which may have a favorable effect on health-resource utilization.

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Keywords: Hospitalization in NMOSD

(DXT33)

Acapella: B-Cell Reconstitution in Ocrelizumab-Treated Patients

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Background: Ocrelizumab (OCR) is a humanized anti-CD20 monoclonal antibody approved for the treatment of relapsing remitting (RRMS) and primary progressive multiple sclerosis (PPMS). In the OPERA trials, circulating CD19+ B-cell counts dropped to zero within 14 days of OCR infusion. Median time to repletion, defined as >79 cells/uL, was 72 weeks (range 27-175 weeks). Up to 5% of patients showed B-cell repletion during treatment. We sought to determine the frequency of patients on OCR who have significant B-cell reconstitution at the time of their next 6-month dose, and to determine if there is a correlation between early B-cell reconstitution and disease breakthrough or adverse events (AEs).

Objectives: As part of the ACAPELLA trial, a prospective study with a primary objective of assessing OCR-associated AEs in a real-world MS population, we sought to evaluate the frequency and duration of early B-cell reconstitution and its relationship to disease activity and AEs.

Methods: All subjects receiving OCR at the Elliot Lewis Center since March 2017 who consented to participate had serum immunoglobulin levels, JCV antibody titers, and lymphocyte subsets on the day of each infusion prior to receiving OCR. Subjects were followed prospectively and monitored for the occurrence of infections and other serious adverse events (SAEs).

Results: As of December 2019, 291 patients had been treated with OCR and enrolled in ACAPELLA: 181 had been treated for at least 12 months, 131 had been treated for 18 months, and 84 subjects had reached 24 months. Of the 291 subjects, 207 had CD19 values drawn at an infusion. One hundred eighteen subjects (57%) displayed ≥1 cell/uL: 81 subjects (39%) had between 1-15 cells/uL, 32 (16%) between 16-79 cells/uL, and 5 (2%) >79 cells/uL. Thirteen patients with B-cell reconstitution at 12 months had early reconstitution with future infusions. Two of the subjects with CD19 values >15 cells/uL experienced clinical or MRI relapse, compared to 8 subjects that did not have B-cell reconstitution.

Conclusions: Although many patients displayed some B-cell repopulation prior to their next dose (113 subjects), CD19 counts of >79 cells/uL were uncommon (5 subjects). Subjects with early B-cell reconstitution at one infusion were likely to continue to show early repopulation at future infusions. Thus far, we have found no significant correlation between B-cell repopulation and either disease activity or adverse events.

Disclosure: *Nothing to disclose.*

Keywords: Disease-modifying treatments in MS, Ocrelizumab

(DXT34)

Revealing the Immune Cell Subtype Reconstitution Profile in Cladribine Treated Patients at the 96 Week Timepoint (CLARITY) Using Deconvolution Algorithms

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Background:
Cladribine tablets (CT) cumulative licensed dose of 3.5mg/kg (CT3.5), administered as two short oral courses over 2 years, transiently reduces total lymphocyte counts, with median values returning to normal range within 11 months and median B cells by 6 months. Clinical efficacy of CT is sustained beyond lymphocyte recovery. Flow cytometric observations suggest long-lasting reductions in memory B cells.

Objectives:
Characterize immune cell transcriptomic signatures in peripheral blood from patients with relapsing-remitting multiple sclerosis during immune repopulation at 96 weeks in the CLARITY study using advanced computational algorithms and correlate these signatures with corresponding flow cytometry data of main lymphocyte subtypes.

Methods:
Gene expression data (U133 Plus 2.0 array) in whole blood samples at 96 weeks were available from patients randomized to placebo (n=57), CT3.5 (n=62) or CT 5.25mg/kg (CT5.25, n=70). These were analyzed with the CIBERSORT deconvolution algorithm (to estimate absolute fractions of 22 immune cell subtypes) and the xCell signature-based method (cell type enrichment analysis for 43 immune cell subtypes). Wilcoxon Rank Sum tests compared between treatment arms. Spearman's rank correlation coefficient was used to measure the relationship between signatures and cell counts. P-values <0.05 were considered nominally significant.

Results:
At 96 weeks, the relative abundance of naïve B cells in CT3.5- and CT5.25-treated patients was significantly higher vs placebo. Plasma cells and class-switched memory B cells were significantly reduced with CT vs placebo. The M2 macrophage signature was significantly enhanced with CT vs placebo. Cell abundance of both naïve and memory CD4+ and CD8+ was significantly reduced with CT vs placebo. Deconvolution signature scores were positively and significantly correlated with corresponding flow cytometry data (r: 0.68–0.72 CD19+ B cells, 0.71 CD4+ T cells, 0.67–0.69 CD8+ T cells).

Conclusions:
At 96 weeks following CT treatment in Year 2, changes in leukocytes suggestive of a shift towards an anti-inflammatory phenotype were detected.

Disclosure: *Irina Kalatskaya, Julie DeMartino, Alex Rolfe: EMD Serono, Inc. (a business of Merck KGaA, Darmstadt, Germany) (salary). Gavin Giovannoni: Abbvie, Actelion, Almirall, Atara Bio, Bayer Schering Pharma, FivePrime, GlaxoSmithKline, GW Pharma, Merck KGaA, Pfizer Inc, Protein Discovery Laboratories, Sanofi-Genzyme, Teva Pharmaceuticals Industries Ltd, UCB, Vertex Pharmaceuticals (consulting fee). Biogen Idec, Ironwood, Merck and Co, Novartis (consulting fee, unrelated research support). Thomas P. Leist: Biogen, EMD Serono, Genentech/Roche, Janssen, Novartis, Teva (consulting fee). Per Soelberg-Sorensen: Biogen (advisory board, research support). Biogen Idec, Sanofi-Aventis (speakers bureau). Genzyme (research support, speakers bureau). GSK (advisory board, steering committees). MedDay Pharmaceuticals (advisory board). Merck KGaA, Novartis, Teva (advisory board, research support, speakers bureau, steering committees). Roche (research support). Ursula Boschert: Merck Serono S.A (a business of Merck KGaA, Darmstadt, Germany) (salary).*

Keywords: Disease-modifying treatments in MS, Immunology and MS

(DXT35)

Real-World Experience with Ocrelizumab - a Safety Analysis

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Background: Ocrelizumab is a humanized monoclonal antibody that selectively targets B-lymphocytes, resulting in their depletion. The FDA approved its use in 2017 for relapsing-remitting and primary-progressive MS. Pooled safety analysis from phase III clinical trials revealed an increase incidence of infection, infusion reaction (IR) and malignancy in ocrelizumab patient groups.

Objectives: We present a real-world safety analysis of ocrelizumab in clinical practice.

Methods: The University of Florida MS Clinic identified subjects as those treated with ocrelizumab prescribed in clinic through electronic medical records. The study collected longitudinal safety laboratories including complete blood count, lymphocyte subset counts and immunoglobulin levels. The study also captured clinical data including disease course, prior disease modifying therapies, IR and occurrence of major clinical events. Analysis of the data assessed trends in laboratories and occurrence of adverse events (AE).

Results: Data from 39 of potential 200 subjects suggests that white blood cell, neutrophil, lymphocyte, and T-cell counts continuously produce the most abnormal results after initiation of ocrelizumab. Nine subjects experienced urinary tract infections, and 2 subjects experienced respiratory tract infections. A case of sepsis and appendicitis resulted in one hospitalization. There were 12 IRs reported, and 1 subject discontinued treatment due to bronchospasms. One subject reported a diagnosis of intraductal carcinoma.

Conclusions: The data reveals that infections and IRs are common amongst patients treated with ocrelizumab, while malignancies occur bur are rare. Of infections, UTIs pose the largest concern,

though respiratory infections and secondary infects also occurred. Although IRs were common, they tended to be acute and easily resolved with the exception of one discontinuation. There is a need for more data to corroborate trends in laboratory values and potential correlation with AEs. Early finding suggest a significant trend in abnormal laboratory values, reported infections and IRs.

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Keywords: Comprehensive care and MS, Disease-modifying treatments in MS, Treatment Safety Analysis in MS

(DXT36)

Effect of Evobrutinib, a Bruton's Tyrosine Kinase Inhibitor, on Immune Cell and Immunoglobulin Levels over 48 Weeks in a Phase 2 Study in Relapsing Multiple Sclerosis

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Background: Bruton's tyrosine kinase (BTK) plays an important role in proinflammatory pathways potentially involved in multiple sclerosis (MS). Consequently, BTK inhibition is being investigated as a potential therapeutic approach for MS. Evobrutinib, a highly selective BTK inhibitor (BTKi), has a dual mechanism of action, impacting both B cells and macrophages through inhibition of B-cell receptor, Fc receptor, and granulocyte–macrophage colony-stimulating factor receptor signaling, and has demonstrated clinical efficacy in MS in a Phase 2 study (NCT02975349; Montalban et al. ECTRIMS 2018 [P322]).

Objectives: To examine the effect of evobrutinib on immune cells and immunoglobulins (Igs) over 48 weeks.

Methods: Patients aged 18–65 years with active relapsing–remitting MS or secondary progressive MS and superimposed relapses were randomized to receive either double-blind evobrutinib (25 mg once daily [qd], 75 mg qd, or 75 mg twice daily), placebo, or open-label dimethyl fumarate 240 mg (reference arm). After 24 weeks, placebo-treated patients were switched to evobrutinib 25 mg qd; other treatment arms continued under original allocation. Safety of evobrutinib, including assessment of B-cell count and Ig level, was a key secondary endpoint; investigations of the effects of evobrutinib on B-cell subsets, T-cell subsets, and natural killer (NK) cells in peripheral blood over 48 weeks were exploratory.

Results: Of 267 patients randomized to treatment, 227 patients completed 48 weeks of treatment. No clinically relevant changes in the number of total B cells, or of memory B, mature naive B, total T, helper T, cytotoxic T, or NK cells, were observed in any evobrutinib treatment group over 48 weeks. No changes in IgG or IgG subtype levels were observed over 48 weeks in any treatment group. At Week 48, there were slight increases from baseline in IgA and reductions in IgM for all evobrutinib groups, which were numerically greater than those with placebo at Week 24.

Conclusions: Patients with MS treated with the BTKi evobrutinib showed no evidence of B-cell depletion or change in mature versus naive B-cell subsets over 48 weeks. IgG levels remained stable and slight elevations in IgA levels were observed. These findings demonstrate that, in contrast to genetic deletion of BTK, continued pharmacologic BTK inhibition does not lead to B-cell depletion or significant reductions in circulating Igs.

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Keywords: Clinical trials, Disease-modifying treatments in MS, Immunology and MS

(DXT37)

Effect of Teriflunomide on Brain Volume Loss in Patients with Relapsing Multiple Sclerosis of Differing Ages in TEMSO

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Background: Teriflunomide significantly reduced brain volume loss (BVL) versus placebo, assessed post hoc using structural image evaluation using normalization of atrophy (SIENA) in patients with relapsing forms of MS (RMS) enrolled in the phase 3 TEMSO study (NCT00134563). It is not known whether the effect of teriflunomide on BVL differs by age.

Objectives: To analyze the effect of teriflunomide treatment on BVL in patients of different age groups with RMS in TEMSO, with a focus on the >45-year age group.

Methods: Patients were randomized 1:1:1 to receive placebo or teriflunomide 7 mg or 14 mg for ≤108 weeks. BVL was assessed as annualized percentage brain volume change (PBVC) from baseline using SIENA at Years 1 and 2 in patients stratified by age: ≤25 years, >25 to ≤35 years, >35 to ≤45 years, and >45 years. Treatment group comparisons of median PBVC values were made via ranked analysis of covariance, adjusted for region, age, EDSS stratum, and baseline normalized brain volume. Data are presented at Year 2 for all patients treated with teriflunomide 14 mg versus placebo, and for patients aged >45 years treated with teriflunomide 14 mg versus placebo.

Results: The median annualized PBVC in all patients was 30.6% lower in the teriflunomide 14 mg group (n=235) versus placebo (n=234; *P*=0.0001). In patients >45 years, the median annualized PBVC was 35.0% lower in the teriflunomide 14 mg group (n=49) versus placebo (n=48; *P*=0.0098).

Conclusions: Teriflunomide decelerated disease-related brain atrophy in RMS patients compared with placebo, including in patients aged >45 years.

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Keywords: Disease-modifying treatments in MS, Imaging and MS, Natural history of MS

(DXT38)

Effects of Ozanimod on Information Processing Speed: Findings from the Phase 3 Sunbeam and Daybreak Extension Trials

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Background: In the phase 3 SUNBEAM study, ozanimod HCl 1 mg improved information processing speed (IPS), measured with the Symbol Digit Modalities Test (SDMT, a component of a secondary endpoint), compared with interferon β-1a (IFN).

Objectives: To evaluate long-term effects of ozanimod, a sphingosine 1-phosphate receptor modulator, on IPS in relapsing multiple sclerosis (RMS) patients.

Methods: In the double-blind, double-dummy, SUNBEAM study (NCT02294058), adults (18–55 years) with RMS were randomized to once-daily oral ozanimod HCl 1 or 0.5 mg, or weekly intramuscular IFN 30 µg. SUNBEAM continued until the last participant was treated for 12 months. Completers were eligible for an open-label extension study (DAYBREAK; NCT02576717) of ozanimod HCl 1 mg. Patients randomized to IFN in SUNBEAM transitioned to ozanimod HCl 1 mg in DAYBREAK 12–24 months after SUNBEAM baseline. This exploratory analysis reports the percentage of participants with clinically meaningful (≥4 point) improvement or worsening of SDMT scores at 12 and 24 months after SUNBEAM baseline in those initially randomized to ozanimod HCl 1 mg or IFN.

Results: In SUNBEAM, 447 participants were randomized to ozanimod HCl 1 mg and 448 to IFN (mean [SD] 13.5 [2.9] months of IFN exposure); of these, 397 and 395, respectively, enrolled in DAYBREAK. Mean (SD) baseline SDMT scores were 47.7 (13.7) and 47.1 (13.5), respectively. At 12 months, 35.6% (152/427) of the ozanimod HCl 1 mg group and 27.9% (119/426) of the IFN group had SDMT improvement; 22.0% (94/427) and 28.2% (120/426), respectively, worsened. At month 24, 41.2% (113/274) of those who received continuous ozanimod HCl 1 mg and 34.5% (91/264) of those originally assigned to IFN in SUNBEAM had SDMT improvement; 21.9% (60/274) and 25.4% (67/264), respectively, worsened relative to SUNBEAM baseline.

Conclusions: In this exploratory analysis, the percentage of participants with SDMT improvement increased over 24 months of continuous treatment with ozanimod HCl 1 mg. The percentage of participants with SDMT improvement was higher at month 24 than month 12

among those who transitioned from IFN to ozanimod HCl 1 mg during the latter 12 months as part of the DAYBREAK study.

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Keywords: Disease-modifying treatments in MS

(DXT40)

Effect of the S1P1/5 Receptor Modulator Ozanimod on Cognitive Processing Speed in Subjects with Relapsing Multiple Sclerosis: Design of the Enlighten Study

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Background: In patients with multiple sclerosis (PwMS), slowed cognitive processing speed emerges as an early deficit. The Symbol Digit Modalities Test (SDMT) is a preferred measure of cognitive performance in PwMS. Ozanimod, an oral sphingosine 1-phosphate (S1P) receptor 1 and 5 modulator, was well tolerated and more effective than weekly intramuscular interferon β-1a (IFN) 30 µg on clinical and MRI endpoints in the phase 3 RADIANCE and SUNBEAM studies. The SUNBEAM study demonstrated a nominally significant (P<0.05) improvement in

SDMT with ozanimod HCl 1 or 0.5 mg/day over IFN 30 µg/week; however, the study was not designed to evaluate SDMT as a primary endpoint.

Objectives: The primary objective of ENLIGHTEN (NCT04140305) is to describe clinically meaningful changes in SDMT (≥4 point or 10% change from baseline) over 3 years in patients with early relapsing MS (RMS) treated with ozanimod HCl 1 mg/day. Secondary objectives are to describe changes from baseline in whole brain and substructure volume; MRI measures of disease activity; patient-reported outcomes (PRO) and quality of life (QOL); disability status based on Timed 25-Foot Walk, 9-Hole Peg Test, and Expanded Disability Status Scale (EDSS); and safety of ozanimod. The study also will explore the correlation between changes in cognitive processing speed and whole brain and substructure volume, and the correlation between changes in cognitive processing speed and PRO and QOL.

Methods: This ongoing multicenter, open-label study is recruiting 250 RMS patients (aged 18–65 years) in the US and Canada. Participants will receive ozanimod HCl 1 mg/day (equivalent to ozanimod 0.92 mg) for 3 years. Key inclusion criteria are diagnosis of MS per 2010 or 2017 McDonald criteria, ≤5 years since diagnosis, ≤1 approved RMS disease-modifying therapy, EDSS score ≤3.5, and no relapse within 30 days of screening. Key exclusion criteria are prior therapy with ozanimod; clinically relevant cardiac, hepatic, neurological, pulmonary, or other chronic conditions; >10 gadolinium-enhancing lesions on baseline brain MRI; or any condition or concomitant medication that might affect cognition or confound test performance.

Results: The ENLIGHTEN study design will be presented. Cognitive performance, disease activity, disability status, and safety will be assessed over 3 years of ozanimod therapy.

Conclusions: This study will determine if ozanimod has a clinically meaningful benefit on cognitive processing speed in patients with RMS.

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Keywords: Cognition and MS, Disease-modifying treatments in MS

(DXT41)

Eculizumab Benefits a Broad Range of Patients with Aquaporin-4 Antibody-Positive Neuromyelitis Optica Spectrum Disorder: The Phase 3 Prevent Study

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Background: Antibodies to the aquaporin-4 (AQP4) water channel in neuromyelitis optica spectrum disorder (NMOSD) are reported to trigger the complement cascade, which is implicated in neuronal injury. The terminal complement inhibitor eculizumab is the first treatment approved for use in patients with AQP4-immunoglobulin G-positive NMOSD, based on data from the PREVENT study.

Objectives: To determine whether eculizumab's beneficial effect in reducing relapse risk in patients with NMOSD is associated with time since diagnosis, relapse history, disability burden or prior immunosuppressant therapy (IST) use, based on data from the phase 3 PREVENT study (NCT01892345).

Methods: In PREVENT, patients received eculizumab (maintenance dose, 1200 mg/2 weeks; n = 96) or placebo (n = 47), with stable-dose concomitant IST (except rituximab and mitoxantrone) permitted. PREVENT was not powered for subgroup analyses; a *post hoc* descriptive analysis was performed on subgroups defined by time since diagnosis, total number of historical relapses, baseline Expanded Disability Status Scale (EDSS) score and prior IST use.

Results: The proportions of patients experiencing an adjudicated relapse were lower with eculizumab than with placebo in all subgroups. Proportions for those receiving eculizumab and placebo, respectively, were: 2/31 (6.5%) versus 6/12 (50.0%) for < 1 year since diagnosis and 1/65 (1.5%) versus 14/35 (40.0%) for ≥ 1 year since diagnosis; 1/39 (2.6%) versus 10/24 (41.7%) for 2–4 historical relapses and 2/57 (3.5%) versus 10/23 (43.5%) for ≥ 5 historical

relapses; 0/14 versus 3/6 (50.0%) for baseline EDSS score ≤ 2.0 and 3/82 (3.7%) versus 17/41 (41.5%) for baseline EDSS score ≥ 2.5 to ≤ 7.0; 0/15 versus 2/5 (40.0%) for no prior IST use (except corticosteroids alone); and 3/81 (3.7%) versus 18/42 (42.9%) for prior IST use. Relapse risk reductions were consistent and statistically significant in all subgroups.

Conclusions: The data from this *post hoc* subgroup analysis suggest that eculizumab reduced relapse risk compared with placebo in patients with AQP4-immunoglobulin G-positive NMOSD, regardless of time since NMOSD diagnosis, relapse history, disability burden or prior IST use.

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Keywords: Eculizumab in NMOSD

(DXT42)

Rationale and Design of Classic-MS Study Evaluating Long-Term Efficacy for Patients with Multiple Sclerosis Treated with Cladribine Tablets

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Background: Cladribine tablets 10 mg (CT; cumulative dose 3.5 mg/kg over 2 years) has demonstrated efficacy versus placebo over 2 years in CLARITY, CLARITY Extension and ORACLE-MS, showing sustained efficacy without further active treatment in CLARITY Extension.

Objectives: CLASSIC-MS will explore long-term efficacy and real-world treatment patterns in patients who participated in these trials. Long-term safety in this population has been assessed in the PREMIERE registry.

Methods: CLASSIC-MS is an exploratory Phase IV study of patients with MS, or those with a first clinical demyelinating event enrolled into the Phase III trials and who received ≥1 course of CT or placebo (N=1946). Following pre-baseline screening and assessment for eligibility, long-term retrospective data will be obtained from medical records at Study Visit 1; prospective data will be collected at Study Visits 1 and 2. Patients will be enrolled for 17 months from approximately Q3 2019 to Q4 2020. Last Patient Last Visit is expected in Q1 2021. Primary objective: evaluation of long-term mobility after treatment with CT or placebo. Secondary objective: assess differences in clinical and magnetic resonance imaging characteristics in long-term responders versus non-responders. Tertiary endpoints: real-world treatment patterns, durability of clinical outcomes, quality of life and cognitive outcomes, influence of high-disease activity on long-term response, differences in genetics between long-term responders and those who are not.

Results: In 2018, a second feasibility survey was sent to 225 centres; 110 centres provided positive responses and were included, representing 48% of sites originally enrolled in the Phase III studies. In total 115 centres were not included (81 were not willing to participate; 13 dropped; 16 were non-responders; 5 were rejected).

Conclusions: CLASSIC-MS will provide valuable information on the long-term efficacy of CT in patients with MS.

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Keywords: Disease-modifying treatments in MS, Management of activities of daily living in MS, Real-world treatment patterns

(DXT43)

Analyses of the Effect of Baseline Age on the Efficacy and Safety of Siponimod in Patients with Active SPMS from the Expand Study

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Background: Siponimod (Mayzent®) is a selective sphingosine 1-phosphate receptor ($S1P_1$ and $S1P_5$) modulator, approved in the USA for treatment of relapsing forms of multiple sclerosis (MS), including clinically isolated syndrome, relapsing-remitting MS and active secondary progressive MS (SPMS). In the phase 3 EXPAND registration trial in SPMS, siponimod significantly reduced risk of 3 month (primary endpoint) and 6 month confirmed disability progression (CDP) by 21% and 26%, respectively.

Objectives: Assess efficacy and safety of siponimod in patients with active SPMS in subgroups of patients aged <45 and ≥45 years (median value) at baseline.

Methods: *Post hoc* analyses were performed in subgroups of patients with active SPMS, defined as a relapse in the 2 years before screening and/or ≥1 T1 gadolinium-enhancing lesion at baseline, randomized to siponimod 2 mg daily or placebo. Efficacy endpoints included: time to 3 and 6 month CDP (as per Expanded Disability Status Scale scores). Adverse events (AEs), serious AEs, and AEs leading to treatment discontinuation were also assessed. Analyses for hypothesis generation only; no adjustment for multiple comparisons.

Results: There were 779 patients with active SPMS: 306 patients aged <45 years (siponimod, n=213; placebo, n=93) and 473 patients aged ≥45 years (siponimod, n=303; placebo, n=170). In those <45 years, siponimod reduced risk of 3 month CDP by 31.9% compared with placebo (siponimod, n=57 [26.8%]; placebo, n=35 [37.6%]; hazard ratio [HR], [95% confidence interval (CI)]: 0.68, [0.45, 1.04]; p=0.0734), and reduced 6 month CDP risk by 39.5% (siponimod, n=44 [20.7%]; placebo, n=30 [32.3%]; HR, [95% CI]: 0.61, [0.38, 0.96]; p=0.0339). In the subgroup of patients ≥45 years, siponimod reduced the risk of 3 month and 6 month CDP by 31.5% and 33.1%, respectively, versus placebo (3 month: siponimod, n=72 [23.8%]; placebo, n=56 [32.9%]; HR, [95% CI]: 0.69, [0.48, 0.97]; p=0.0340; 6 month: siponimod, n=55 [18.2%]; placebo, n=44 [25.9%]; HR, [95% CI]: 0.67, [0.45, 1.0]; p=0.0471). Siponimod was generally well tolerated in both subgroups. Rates of any AE were similar for siponimod and placebo in patients <45 years (82.6% vs 82.8%), and slightly higher for siponimod in those ≥45 years (89.8% vs 75.9%). Rates of AEs and AEs leading to discontinuation were similar between groups.

Conclusions: In EXPAND, siponimod provided similar clinical effects in reducing CDP risk in patients aged <45 years and ≥45 years with active SPMS.

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Keywords: Disease-modifying treatments in MS

(DXT44)

Real-World Patterns of Disease Progression in Patients with Multiple Sclerosis Who Are Adherent Versus Non-Adherent to Disease Modifying Treatments over 6 Years

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Background: Multiple sclerosis (MS) is a chronic disease that requires long-term treatment for most patients. Disease modifying treatment (DMT) adherence is often an issue for MS patients and evidence suggests that non-adherence can impact outcomes. Data is needed to understand the impact of long-term DMT use on clinical outcomes.

Objectives: To assess the impact of long-term DMT adherence on MS disease progression in the real-world.

Methods: A retrospective cohort analysis of MarketScan Commercial enrollees from 2011–2017 was performed. MS was defined as ≥3 ICD-9/10 (340/G35) diagnosis claims or ≥1 diagnosis and ≥1 DMT claim (age 18 and 65 years at index) with index-date being the first diagnosis or DMT claim in 2012. Continuous enrollment started from 1 year pre-index, with a follow-up of ≥3 years of continuous enrollment and up to 6 years. Adherent-users as medication possession ratio (MPR) ≥0.8 in follow-up, and non-adherent users as 0<MPR<0.8. Propensity score greedy matching was used to balance population characteristics (age, gender, geography, comorbidities, relapses) 1 year pre-index. We compared the average number of relapses, defined as a hospitalization with a primary diagnosis of 340/G35 or an outpatient visit with diagnosis of 340/G35 plus a pharmacy or medical claim for a qualifying corticosteroid within 7 days, between two cohorts using Poisson regression model. We also compared the time to first relapse, time to cane/walker use, and time to wheelchair use between two cohorts using Cox-proportional hazard model.

Results: 15,617 MS patients were identified (42% adherent, 43% non-adherent, 15% non-DMT treated). Of them, 6121 propensity score matched pairs were analyzed. Standardized differences of all baseline characteristics between two comparison groups were <0.1. Adherent users had significantly lower average number of relapses (0.153) than non-adherent (0.201) users (annualized relapse rate ratio: 0.76, 95% confidence interval [CI]: 0.74-0.79, p<0.001). Adherent

users had significantly longer time to first relapse (hazard ratio [HR]=0.82, 95% CI: 0.77-0.87, p<0.001), cane/walker use (HR=0.81, 95% CI: 0.71-0.93, p=0.003), and wheelchair use (HR=0.60, 95% CI: 0.51-0.70, p<0.001).

Conclusions: This study highlights the importance of DMT adherence in slowing disease progression. Indicators of MS-related disability were found to be related to adherence, suggesting a lower rate of disability progression over time. Further research is needed to better understand barriers of adherence with DMTs.

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Keywords: Disease-modifying treatments in MS

(DXT45)

Pharmacist-Based Intervention for Improving Baseline Laboratory Monitoring for Patients on Multiple Sclerosis Disease Modifying Therapies

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Background: Disease Modifying Therapies (DMTs) require baseline labs prior to initiation. Under our institution's pharmacotherapy protocol, clinical pharmacy specialists may order labs based on their assessment of the patient's monitoring needs. Currently, there is no standardized clinical practice guideline for ordering appropriate labs prior to initiating medications prescribed for patients with MS. Frequently, baseline labs are not available in the chart, making it challenging to determine treatment and evaluate safety. A standardized process, including the utilization of the pharmacotherapy protocol, would optimize safety and guide clinical decisions regarding the management of patients prescribed DMTs for MS.

Objectives: The percentage of appropriate labs drawn for the specified DMTs following the implementation of a standardized operating protocol in the MS outpatient neurology clinic.

Methods: A clinical practice guideline was implemented on 10/1/19, outlining the baseline labs required within six months prior to initiation of specific DMTs. The following DMTs were included in the guideline: interferon beta-1a, peginterferon beta-1a, dimethyl fumarate, and teriflunomide. All patients who had a medication prescribed for the listed DMT from 10/1/18 to 3/31/19 were included in the baseline analysis. The clinical pharmacy specialist utilized the pharmacotherapy protocol to order appropriate labs when a therapy was initiated. A post analysis

was performed to compare rates of appropriate labs drawn in all patients who had a prescription for the DMTs listed above, from 10/1/19 to 3/31/20. The patients included were those starting DMT for the first time, changing to a new DMT, or restarting a DMT after being off therapy for > 6 months.

Results: (Preliminary) Of the 43 patients prescribed a DMT during the baseline analysis, 13 (30.2%) patients had all appropriate labs drawn within 6 months. Of the remaining 30 (69.8%) patients who did not have all appropriate labs drawn, 18 (60%) patients had no labs documented in the chart within the last 6 months. The most common labs not drawn include differential (83.3%), LFTs (63.3%), and CBC (56.6%). Since the implementation of the clinical practice guideline, 75% of patients have had all appropriate labs drawn within 6 months of therapy initiation. However, baseline labs have been collected on 100% of patients, with only the differential not drawn.

Conclusions: Integration of a clinical pharmacy specialist in the management of patient safety is crucial to delivering exceptional care. Implementation of a standardized operating procedure and incorporation of pharmacists to assist in the monitoring of patients, contributed to an increase in appropriate labs drawn prior to initiation of DMT. Additionally, the utilization of pharmacists practicing in multidisciplinary settings to further elevate the level of care provided to patients could be extrapolated to other clinic areas and disease states.

Disclosure: *Nothing to disclose.*

Keywords: Comprehensive care and MS, Disease-modifying treatments in MS, PHARMACIST

(DXT46)

Cognitive Performance and Disability Across Age Groups in Teriflunomide-Treated Patients in the Teri-PRO Study

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Background: The Teri-PRO study (NCT01895335) evaluated patient-reported outcomes, including cognition, in teriflunomide-treated patients with relapsing forms of MS in a real-world setting. It is unknown whether treatment effects on cognitive performance are influenced by patient age and/or physical disability.

Objectives: To evaluate the effects of teriflunomide treatment on cognition across age groups, in the context of disability.

Methods: Teri-PRO was a phase 4, multicenter, prospective, single arm, open-label, real-world study assessing treatment satisfaction of teriflunomide 7 mg or 14 mg over 48 weeks using patient-reported outcomes. Cognitive performance, measured using the Symbol Digit Modalities Test (SDMT), and disability, assessed with the EDSS, were secondary endpoints. The SDMT was scored as the proportion of correct responses (scale 0−1). Patient improvement was computed as the change in score from baseline to 48 weeks; Spearman correlation assessed the relationship between SDMT and EDSS outcomes.

Results: SDMT and EDSS data were available in 839 patients (≤25 years: n=21; >25 to ≤35 years: n=105; >35 to ≤45 years: n=243; >45 to ≤55 years: n=279; and >55 years: n=191). Baseline mean SDMT scores across all age groups were similar (≤25 years: 0.99; >25 to ≤35 years: 0.98; >35 to ≤45 years: 0.98; >45 to ≤55 years: 0.97; and >55 years: 0.97), and remained stable through Week 48 (least squares mean change ranged from -0.01 to +0.01 across groups). At baseline, mean EDSS scores were higher with advancing age, from 1.52 in patients ≤25 years to 4.12 in patients >55 years. Least squares mean EDSS changes from baseline to Week 48 were not significant, except in patients >45 to ≤55 years (+0.13, *P*=0.0079). Cognition and disability were not correlated in any age group (Spearman correlations, ≤25 years: -0.28, *P*=0.2; >25 to ≤35 years: 0.02, *P*=0.9; >35 to ≤45 years: -0.09, *P*=0.2; >45 to ≤55 years: -0.05, *P*=0.4; >55 years: 0.04, *P*=0.6) or in the overall population (-0.034, *P*=0.3).

Conclusions: Across all age groups, patients in Teri-PRO had similarly high cognitive function at baseline, and cognitive performance after 48 weeks of teriflunomide treatment was stable. SDMT and EDSS were not significantly correlated.

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Keywords: Aging and MS, Cognition and MS, Disease-modifying treatments in MS

(DXT48)

Efficacy of Subcutaneous Interferon Beta-1a in Patients With a First Clinical Demyelinating Event: REFLEX Study - Outcomes in Patients Stratified by 2017 McDonald Criteria

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Background: The REFLEX (REbif FLEXible dosing in early multiple sclerosis [MS]) trial demonstrated that subcutaneous interferon β-1a (sc IFN β-1a) reduced conversion to MS (McDonald 2005 criteria) and to clinically definite MS (CDMS) versus placebo in patients with a first clinical event suggestive of MS. A retrospective analysis of the study showed that the overall results were unchanged by the application of the McDonald 2010 MS criteria. The revised 2017 McDonald MS criteria include the presence of cerebrospinal fluid–specific oligoclonal bands, symptomatic lesions, and cortical lesions to aid MS diagnosis.

Objectives: Assess the effects of sc IFN β-1a on time to McDonald 2005 criteria MS (time to next relapse, Expanded Disability Status Scale [EDSS] progression, or MS-related MRI lesion or lesions) and CDMS (time to relapse or EDSS progression), and annualized relapse rate (ARR) during REFLEX, stratified by retrospective diagnosis at baseline in patients that either meet or do not meet the updated McDonald 2017 MS criteria.

Methods: During REFLEX, patients were randomized to either sc IFN β-1a three times weekly (tiw) or once weekly (qw), or placebo, for 2 years. This retrospective analysis stratified patients randomized to the intent-to-treat population in REFLEX into McDonald 2017–positive (defined as those that retrospectively met the 2010 McDonald MS criteria at baseline or those with positive oligoclonal bands) and McDonald 2017–negative subgroups. Kaplan–Meier curves were used to estimate time to McDonald 2005 MS and time to CDMS by treatment group and for each McDonald 2017 subgroup.

Results: As the detection of oligoclonal bands was optional during REFLEX, only a small number of patients were added from the McDonald 2010 analysis. A total of 235/517 patients were classed as McDonald 2017–positive at baseline (40 of whom were McDonald 2010–negative but had positive oligoclonal bands). In the McDonald 2017–positive subgroup, treatment with sc IFN β-1a tiw or qw significantly delayed time to McDonald 2005 MS (tiw vs

placebo hazard ratio [HR]=0.47, p<0.001; qw vs placebo HR=0.58, p=0.002) and CDMS (tiw vs placebo HR=0.46, p=0.010; qw vs placebo HR=0.42, p=0.003) versus placebo. Treatment with sc IFN β-1a qw or tiw significantly reduced mean ARR versus placebo in McDonald 2017–positive patients (reductions of 69.1% and 59.3%, respectively; p<0.001).

Conclusions: The treatment effects of sc IFN β-1a observed in McDonald 2010 patients on time to McDonald 2005 MS and CDMS were maintained in the McDonald 2017–positive subgroup, although there were only a small number of additional patients when the 2017 criteria were applied.

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Keywords: Diagnosis, Biomarkers, Disease-modifying treatments in MS

(DXT49)

Post Hoc Analysis of Efficacy of Cladribine Tablets in Patients with Relapsing-Remitting Multiple Sclerosis Aged over and Under 30 Years in the Clarity Study

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Background:
Efficacy of cladribine tablets 3.5 mg/kg (CT3.5, cumulative dose over 2 years [yrs]) has been reported in relapsing-remitting multiple sclerosis (RRMS) in the 96-week (wk) CLARITY study. Prior *post hoc* analyses of CLARITY found that CT3.5 treatment resulted in similar benefits

across the age spectrums of the studied patients (pts) in risk reduction of relapse and odds of remaining free from disease activity.

Objectives:
This *post hoc* analysis further examined efficacy outcomes of CT3.5 in CLARITY pts aged ≤30 and >30 yrs at study enrollment.

Methods:
Analyses were performed by treatment (CT3.5 vs PBO) and age subgroup (≤30 and >30 yrs), a relatively young age cut-off with adequate N needed for analyses. Endpoints were relapse (relapse free status and annualized relapse rate [ARR]), 3- and 6-month (mo) confirmed disability progression (CDP, based on Expanded Disability Status Scale), MRI activity, and No Evidence of Disease Activity (NEDA) status (no relapse, 3- or 6-mo CDP, or MRI activity). P-values are nominal.

Results:
This analysis was carried out in 870 pts: ≤30 yrs: CT3.5 N=109, PBO N=102; >30 yrs: CT3.5 N=324, PBO N=335. In both age subgroups, CT3.5 significantly reduced adjusted ARR (95% confidence interval [CI]) (≤30 yrs: 0.16 [0.11–0.23] vs 0.48 [0.38–0.60]; >30 yrs: 0.15 [0.12–0.18] vs 0.31 [0.27–0.37]; P<0.0001), and increased the number of pts who were relapse-free through Wk 96 (≤30 yrs: 73.4% vs 44.1%; >30 yrs: 76.2% vs 57.3%) vs PBO. CT3.5 treatment increased the odds of being free from 3- or 6-mo CDP through Wk 96 (3-mo CDP at Wk 96 in both age subgroups: 0.84–0.88 vs 0.76 [both subgroups]; 6-mo CDP at Wk 96: 0.89–0.94 vs 0.83–0.86) vs PBO. CT3.5 also significantly reduced the adjusted mean (95% CI) cumulative number of new T1 gadolinium-enhancing (≤30 yrs: 0.22 [0.15–0.33] vs 1.37 [0.97–1.93]; >30 yrs: 0.05 [0.03–0.08] vs 0.77 [0.61–0.98]) and active T2 (≤30 yrs: 0.68 [0.53–0.88] vs 2.20 [1.73–2.81]; >30 yrs: 0.26 [0.21–0.32] vs 1.19 [1.01–1.41]) lesions, and increased the number of pts achieving NEDA status using 3-mo (≤30 yrs: 30.3% vs 2.9%; >30 yrs: 44.4% vs 17.3%) or 6-mo (≤30 yrs: 30.3% vs 2.9%; >30 yrs: 46.3% vs 17.9%) CDP vs PBO (all P<0.0001) at 96 wks.

Conclusions:
CT3.5 treatment improved clinical and MRI outcomes in both younger and older pts in CLARITY. Relapse and disability outcomes appeared mostly similar between the age subgroups; however, >30 yrs age subgroup appeared to have a greater reduction in MRI lesion activity and a higher rate of achieving NEDA status.

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Keywords: Disease-modifying treatments in MS

(DXT50)

Prevalence of Serious Adverse Pregnancy Outcomes after Exposure to Interferon Beta before or during Pregnancy: Stratification By Characteristics of Pregnant Women with MS in a Register-Based Cohort Study in Finland and Sweden

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Background: A recent cohort study in women with multiple sclerosis (MS) reported no increase in the prevalence of adverse pregnancy outcomes after exposure to interferon beta (IFN β) before or during pregnancy. However, differing prevalence by maternal characteristics is unknown.

Objectives: To describe the prevalence of serious adverse pregnancy outcomes (SAPOs) among pregnant women with MS exposed to only IFN β and those unexposed to any MS disease-modifying drugs (DMDs), with stratification by maternal characteristics.

Methods: This cohort study extracted register data from Finland (1996–2014) and Sweden (2005–2014) on pregnant women with MS who were 1) dispensed only IFN β within 6 months before the last menstrual period (LMP) or during pregnancy (IFN β–exposed, n=718 pregnancies) and 2) without dispensed MS DMDs (unexposed, n=1397 pregnancies). The prevalence (%) of SAPOs (consisting of elective terminations due to fetal anomaly, major congenital anomalies in live birth, and stillbirth) with 95% confidence intervals (CIs) was analyzed with stratification by maternal characteristics at LMP: time since MS diagnosis, duration of MS treatment, maternal age, and presence of chronic disease.

Results: The prevalence of SAPOs appeared similar among the IFN β–exposed and unexposed groups when MS was diagnosed ≤2 years (0.9%, 95% CI 0.1–3.2% vs 3.0%, 1.6–5.2%) or 3–5 years (2.4%, 0.9–5.1% vs 6.0%, 4.0–8.6%) before LMP, and was comparable for >5 years (3.3%, 1.4–6.4% vs 3.0%, 1.7–4.8%). When stratified by duration of MS treatment, the

prevalence among the IFN β–exposed versus unexposed with ≤2-year treatment was 1.3% (0.4–3.4%) versus 4.6% (2.9–6.9%), 3–5-year treatment 1.7% (0.5–4.4%) versus 4.9% (2.9–7.7%), and >5-year treatment 4.3% (1.9–8.3%) versus 2.7% (1.2–5.0%). The prevalence was similar among the IFN β–exposed versus unexposed in strata by maternal age (≤20, 21–25, 26–30, 31–35, 36–40, >40 years) and presence of chronic diseases (yes/no).

Conclusions: In this population-based observational study, the descriptive prevalence of SAPOs appeared similar with IFN β exposure before or during pregnancy, when pregnant women with MS were stratified by maternal characteristics.

Disclosure: *Marta Korjagina, Katja Hakkarainen, Riho Klement, Pasi Korhonen: EMD Serono (contracted research). Marta Korjagina, Pasi Korhonen: StatFinn-EPID Research (salary). Katja Hakkarainen, Riho Klement: StatFinn-EpidResearch (salary). Sarah Burkill, Shahram Bahmanyar: Centre for Pharmacoepidemiology (salary). Yvonne Geissbuehler: Novartis Pharma AG (salary). Meritxell Sabidó: Merck KGaA (salary). Achint Kumar: Biogen (salary). Kiliana Suzart-Woischnik: Bayer AG (salary). Jan Hillert: Bayer-Schering, Biogen, Merck Serono, Novartis, Sanofi-Genzyme, Teva (consulting fee, speakers bureau). Bayer-Schering, Biogen, Merck Serono, Novartis, Sanofi-Genzyme, Teva, Swedish Research Council, Swedish Brain Foundation (contracted research). Auli Verkkoniemi-Ahola: Biogen, Genzyme, Grifols, Merck, Novartis, Roche, Sanofi (consulting fee, speakers bureau). Sanofi (contracted research). Scott Montgomery: AstraZeneca, IQVIA, Novartis, Roche (contracted research). Teva (speakers bureau).*

Keywords: Disease-modifying treatments in MS, MS and the caregiver/family, Pregnancy and MS

(DXT51)

High Rates of Adherence to Oral Diroximel Fumarate and Dimethyl Fumarate Are Observed and Sustained in RMS Patients

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Background: Adherence to therapy in multiple sclerosis (MS) leads to improved clinical outcomes. Persistence to therapy and discontinuation rates contribute to adherence. Diroximel fumarate (DRF) is a novel oral fumarate recently approved in the United States for relapsing forms of MS, administered as 2 capsules twice daily (BID).

Objectives: To compare adherence with DRF vs dimethyl fumarate (DMF) in EVOLVE-MS-2 and describe long-term adherence and efficacy outcomes with DRF in EVOLVE-MS-1.

Methods: Adherence was assessed in patients with relapsing-remitting MS who received DRF or DMF in the 5-week, randomized EVOLVE-MS-2 study (NCT03093324) and in those who received DRF in the ongoing, 96-week, open-label EVOLVE-MS-1 study (NCT02634307). All EVOLVE-MS-2 patients received 2 capsules BID. Adherence was determined by pill count (number taken divided by the number prescribed x 100). In patients who discontinued treatment, adherence was based on duration of treatment and not the full study period. Efficacy outcomes were assessed in EVOLVE-MS-1.

Results: In the completed EVOLVE-MS-2 study, mean adherence was high (DRF 97.1%, n=252; DMF 97.0%, n=251); 97.4% of patients were ≥80% adherent to therapy. Discontinuation rates were lower with DRF (3.2%) than DMF (7.2%), primarily due to differences in GI tolerability. In EVOLVE-MS-1 as of November 30, 2018 (median [range] exposure, 84 [0-100] weeks; n=888), mean adherence was 93.4% (n=877); 92.0% of patients were ≥80% adherent. Overall, 16.3% of patients discontinued treatment. Median (range) exposure for patients with ≥80% vs <80% adherence was 84 (1-100) and 22 (0-97) weeks, respectively. In patients with ≥80% adherence, adjusted annualized relapse rate was 0.15 (95% CI 0.13-0.19), representing a 79.4% (95% CI 75.0-83.0; p<0.0001) reduction from the 12 months before study entry. Mean (SD) change in EDSS score from baseline to Wk96 in patients with ≥80% adherence was 0.07 (0.59; n=310). The small sample size (n=70 at baseline, n=2 at Wk96) of patients with <80% adherence limits the ability to draw conclusions on the correlation between adherence and efficacy outcomes.

Conclusions: High adherence and low discontinuation rates demonstrate documented treatment adherence and persistence to DRF. Adherence rates with DRF and DMF in EVOLVE-MS-2 were sustained in DRF-treated patients from EVOLVE-MS-1 for up to 96 weeks, demonstrating little impact of a 2 capsules BID dosing regimen. DRF-treated patients in EVOLVE-MS-1 had improved efficacy outcomes from baseline.

Support: Biogen

Disclosure: *Mary Kay Fink: Biogen, EMD Serono, Novartis (speakers bureau). Biogen, Novartis, and Sanofi-Genzyme (scientific advisory board). Elzbieta Jasinska: Biogen (scientific advisory boards). Novartis, Allergan, Hoffman La-Roche,Teva, Adamed, Polfarma (speakers bureau). Pavle Repovic: Alexion, Biogen, Celgene, EMD Serono, Novartis, Sanofi-Genzyme, Viela (consulting fee). Alexion, Biogen, Genzyme, Genentech, EMD Serono (speakers bureau). Biogen, Genentech, EMD Serono (contracted research). Cortnee Roman: Alexion, Biogen, Bristol Myer Squibb, Genentech, Novartis, Sanofi-Genzyme (speakers bureau). Alexion, Biogen, Bristol Myers Squibb, EMD Serono, Genentech, Novartis, Sanofi-Genzyme. (consulting fee). Biogen, Bristol Myer Squibb, Genentech, Novartis, Sanofi-Genzyme (advisory boards). Hailu Chen, Shivani Kapadia: Biogen (ownership interest, salary). Sibyl Wray: Alkermes Inc, Biogen, Cellgene, Genentech/Roche, Sanofi/Genzyme, Novartis, TG Therapeutics (contracted research). Biogen, EMD Serono, Genentech/Roche, Sanofi/Genzyme (consulting fee, speakers bureau).*

Keywords: Disease-modifying treatments in MS, Medication adherence

(DXT52)

Efficacy and Safety of Eculizumab in Patients with Neuromyelitis Optica Spectrum Disorder Previously Treated with Rituximab: The Phase 3 Prevent Study

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Background: In the PREVENT study, eculizumab was associated with a significant reduction in relapse risk versus placebo and was well tolerated. In total, 46 patients (26/96 receiving eculizumab, 20/47 receiving placebo) had been previously treated with the monoclonal antibody rituximab.

Objectives: To describe the efficacy and safety of eculizumab in patients in the randomized, double-blind, placebo-controlled, phase 3 PREVENT trial (NCT01892345) who had previously received rituximab.

Methods: Adults with aquaporin-4 immunoglobulin G-positive neuromyelitis optica spectrum disorder received eculizumab (maintenance dose, 1200 mg/2 weeks) or placebo with/without concomitant immunosuppressive treatment (except rituximab/mitoxantrone). A *post hoc* descriptive analysis was performed using data from patients with any prior rituximab treatment (within the previous year only for review of adverse events [AEs]) recorded more than 3 months before randomization.

Results: Baseline characteristics of the prior-rituximab subgroup were similar to the total PREVENT population; however, the subgroup included a lower proportion of Asian patients (10.9% vs 36.4% in total PREVENT study population) and greater representation from the Americas (58.7% vs 30.8%). In the subgroup, median times from last dose of rituximab to

meningococcal vaccination and to first dose of study treatment were 31.7 and 38.7 weeks, respectively. Adjudicated relapses occurred in 1/26 (3.8%) and 7/20 (35.0%) patients in the eculizumab and placebo arms, respectively (hazard ratio 0.093; 95% confidence interval 0.011–0.755; $p = 0.0055$). AE rates in patients receiving eculizumab and placebo within 1 year of previous rituximab use were 1025.8 and 1029.1 events/100 patient-years (both 100% of patients), respectively; rates of serious AEs were 46.9 and 66.0 events/100 patient-years (38.9% and 47.1% of patients), respectively. Serious infections/infestations were recorded in 2/18 (11.1%) and 2/17 (11.8%) patients in the eculizumab and placebo arms, respectively.

Conclusions: In patients with aquaporin-4 immunoglobulin G-positive neuromyelitis optica spectrum disorder in PREVENT who had previously received rituximab, the risk of adjudicated relapse was significantly lower with eculizumab than with placebo. Rates of serious infections were similarly low with eculizumab and placebo.

Disclosure: *Michael Levy: Alexion Pharmaceuticals (consulting fee, contracted research, fees for non-cme/ce services received directly from commercial interest or its agent). Genentech, Quest Diagnostics, Viela Bio (consulting fee, fees for non-cme/ce services received directly from commercial interest or its agent). Achim Berthele: Alexion Pharmaceuticals (consulting fee, contracted research, fees for non-cme/ce services received directly from commercial interest or its agent, speakers bureau). Ho Jin Kim: Alexion Pharmaceuticals, Celltrion, Eisai, HanAll BioPharma, Merck Serono, Novartis, Sanofi Genzyme, Teva-Handok, Viela Bio (consulting fee). Journal of Clinical Neurology (is an associated editor). MedImmune/Viela Bio (serves on a steering committee). Multiple Sclerosis Journal (is a co-editor). Kazuo Fujihara: Alexion Pharmaceuticals, Biogen, Chugai, Mitsubishi-Tanabi, Novartis (consulting fee, fees for non-cme/ce services received directly from commercial interest or its agent). Asahi Medical, Bayer, Eisai, Roche, Teijin (fees for non-cme/ce services received directly from commercial interest or its agent). Ichiro Nakashima: Alexion (consulting fee). Celia Oreja-Guevara: Alexion Pharmaceuticals, Merck, Novartis, Roche, Sanofi (consulting fee, contracted research). Jacqueline Palace: Biogen, Chugai (contracted research). LEK, Viela Bio, Guidepoint (consulting fee). Merck Serono (meeting/lecture/workshop participation). Novartis, Roche, Argenx (speakers bureau). UCB, Viela Bio, Roche (conference/lecture participation). Sean J. Pittock: Alexion Pharmaceuticals (all compensation related to alexion pharmaceuticals is paid directly to mayo clinic, consulting fee, contracted research). Astellas (all compensation related to astellas is paid directly to mayo clinic, consulting fee). Autoimmune Encephalitis Alliance (all compensation related to autoimmune encephalitis alliance is paid directly to mayo clinic is paid directly to mayo clinic, contracted research). Grifols (all compensation related to grifols is paid directly to mayo clinic, contracted research). MedImmune (all compensation related to medimmune is paid directly to mayo clinic, consulting fee, contracted research). UCB (consulting fee, dr. pittock received personal compensation for attending the ucb advisory board meeting in stockholm, sweden on september 10, 2019.). Murat Terzi, Shanthi Viswanathan, Kai-Chen Wang: Nothing to disclose. Natalia Totolyan: Alexion, Janssen, Novartis, Roche, Sanofi, Receptos Inc, Biocad (Russia) (contracted research). Merck (consulting fee). Roche, Sanofi (fees for lectures). Amy Pace, Marcus Yountz, Eva Laudon-Meyer: Alexion Pharmaceuticals (ownership interest, salary). Diane Lawson: Alexion Pharmaceuticals (salary). Dean Wingerchuk: MedImmune, Novartis, Biogen, Celgene, Genentech, TG Therapeutics, Arcus Medica, Reistone (consulting fee). Terumo BCT, Alexion Pharmaceuticals (fees for non-cme/ce services received directly from commercial interest or its agent).*

Keywords: Eculizumab in NMOSD

(DXT53)

MS Clinical Phenotypes: Using Technology to Educate Patients and Optimize Treatment

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Background:

The evolution of new clinical phenotype descriptions for relapsing and progressive forms of MS by the MS Phenotype Group and new guideline recommendations for disease-modifying therapies have delineated optimal treatments for each clinical phenotype.[1,2,3]

The Multiple Sclerosis Association of America (MSAA) and @Point of Care have collaborated to develop complementary apps for use by patients and their clinicians that facilitate sharing of data: *My MS Manager* ™, a HIPAA compliant patient app, and Multiple Sclerosis @Point of Care, a clinician app. It was important to enhance the *My MS Manager* app to provide education addressing MS phenotypes and their implications, and a field for patients to enter their phenotype.

Objectives:

Encourage MS patients to know their phenotype, clinical course, and implications for treatment for discussion with their clinician and caregivers.

Methods:

MSAA and @Point of Care collaborated to enhance the *My MS Manager* app to include additional fields for the collection of clinical phenotypes, to assess how many did/did not know their clinical phenotype and evaluate other patterns. A video was developed to increase patients' awareness about the importance of knowing their clinical phenotype and how this guides treatment options.

Results:

Of 3765 patients who filled in their clinical phenotype on the *My MS Manager* app:

- 20% (744) did not know their clinical phenotype and those unsure of their phenotype were younger
    - *Implication*: Patients, especially those younger, need to understand the importance of knowing their phenotype and its implications for long-term treatment
- Thousands of MS patients viewed the educational videos addressing MS and clinical phenotype information

  - *Implication*: Patients want to gain insights into their MS and clinical phenotypes
- Of 55 PPMS patients, 25% were not receiving an FDA-approved therapy nor were they enrolled in a PPMS clinical trial
  - *Implication*: Better informed PPMS patients and clinicians may opt for FDA-approved therapies or clinical trials

Conclusions:

The *My MS Manager* patient app facilitates MS patients' ability to record their clinical phenotype, access educational videos – including those addressing phenotype, and empower them to better understand MS phenotypes and implications for treatment choices for discussion with their clinicians. This will ensure optimal treatment choices.

Disclosure: *Nothing to disclose.*

Keywords: Comprehensive care and MS, Disease-modifying treatments in MS, MS Phenotypes

(DXT54)

Assessment of the Discontinuation Rates of Disease Modifying Therapy in Veterans with Multiple Sclerosis

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Background: Disease-modifying therapy (DMT) is the preferred treatment approach for multiple sclerosis (MS) and has been shown to reduce the rate of relapse and slow disease progression. Poor adherence is associated with an increased risk of relapse leading to an increase in morbidity outcomes as well as overall costs in MS patients. We conducted a retrospective chart review to improve our understanding of the reasons for discontinuation of DMTs, the impact of adverse drug reactions (ADRs) on the rate discontinuation of DMTs and identify barriers to adherence.

Objectives: To examine the discontinuation rates and the reasons for discontinuation of DMTs among veterans with MS.

Methods: We conducted a retrospective chart review of veterans with MS seen in the MS Clinic and General Neurology Clinic at Veterans Affairs Greater Los Angeles Healthcare System (VAGLAHS) who were on DMTs from 1/1/2010 to 12/31/2019. Demographic data and the following data points were collected: past medical history, date of diagnosis, duration of MS,

characteristics related to DMT use such as prescription refill history, reason for discontinuation, duration of medication use, and response to DMTs.

Results: To date we have screened 100 electronic medical records of veterans with MS on DMTs. We documented 220 trials of DMT in 100 patients enrolled in our study. Among these 100 patients, the most commonly prescribed DMTs were interferon-beta and glatiramer acetate. Adherence rates observed were highest among veterans on infused DMTs and lowest among veterans on injectable DMTs. Approximately 20% of patients discontinued the injectable DMTs due to inefficacy, compared to 10% for oral DMTs and 10% for infused DMTs. Injectable DMTs were discontinued in 20% of veterans due to ADRs, compared to 18% for oral DMTs and 4% for infused DMTs. Data collection is ongoing and may help us identify barriers to DMT adherence in veterans with MS.

Conclusions: Preliminary results of our study suggest differences in adherence to DMTs and possible reasons for discontinuation of DMTs in veterans with MS.

Disclosure: *Naomi Wu, Jeremy Liu, Christine Lava, Hyojin Suh, Andrea Hanssen, Sunita Dergalust: Nothing to disclose. Eric Williamson: Novartis Pharmaceuticals (contracted research).*

Keywords: Disease-modifying treatments in MS, medication adherence

(DXT55)

Herpes Zoster Virus (HZV) Infections Among Multiple Sclerosis Patients Treated with Various Disease Modifying Therapies

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Background:

Disease modifying therapies (DMTs) for multiple sclerosis (MS) may increase the risk for opportunistic infections, including herpes zoster (HZV). The relative frequency of HZV infection in the treated MS population is unknown. Furthermore, the relative distribution of reported cases per age group and gender is unknown.

Objectives:

To stratify the frequency of voluntarily reported HZV infections by DMT, age, and gender in MS patients.

Methods:

We queried the Food and Drug Administration Adverse Event Reporting System (FAERS) for adverse events ("herpes zoster" and "varicella") reported in MS patients between January 1999 and June 2019 receiving interferon beta (IFB), glatiramer acetate (GA), natalizumab (NAT), fingolimod (FIN), teriflunomide (TER), dimethyl fumarate (DMF), alemtuzumab (ALE), and ocrelizumab (OCR). We excluded reports where the "suspect drug" included two or more DMTs. We stratified the reports for each DMT, by year of report, age and gender.

Results:

3352 reports met our inclusion criteria. Annual report rates [mean (SD)] were highest for patients treated with NAT 81.9(91.9), and lowest for GA 2.1(2.5). Other DMTs: FIN 70.3(27.3); DMF 66(21); OCR 55.3(27.8); ALE 22.8(15); INF 22.6(18); TER 10.4(4.7). Reports were 4.7x more in females (ranging from 2.3x for ALE to 8.2x for IFB). The highest percentage of reports was in the sixth decade of life for all DMTs except ALE (fourth decade). Several reports were in individuals younger than 40 (25.0%).

Conclusions:

Reports of HZV infections varied based on the DMT used, patient age, and gender. HZV reports were nearly five fold more frequent in females than males, and reports among patients younger than 40 were higher than expected. Database limitations precluded calculations of incidence. We encourage further investigations of the incidence and risk mitigation strategies (including vaccination practices) of HZV in MS patients on DMTs regardless of age of the patient.

Disclosure: *Nicola Carlisle, Sam I. Hooshmand, Michelle Maynard, Leah Hoffman: Nothing to disclose. Ahmed Z. Obeidat: Alexion, Biogen (consulting fee, speakers bureau). Celgene, EMD serono, Genentech, Sanofi (consulting fee). International journal of MS (editorial board). Novartis (speakers bureau).*

Keywords: Disease-modifying treatments in MS, TYPE NEW KEYWORD HERE

(DXT56)

Potential Weight Changes Among Patients with Multiple Sclerosis Undergoing Treatment with Ocrevus (Ocrelizumab)

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Background: Ocrelizumab (Ocrevus), approved for use in 2017, has quickly become a formidable disease modifying therapy (DMT) option for multiple sclerosis (MS). While effective, potential side effects from ocrelizumab are still being explored, such as weight changes.

Objectives: 1) To examine if patients have experienced weight changes while receiving ocrelizumab and 2) to explore associations between changes in weight and patients' demographic and clinical characteristics.

Methods: Data were extracted from the medical records of 152 patients from who had recorded weights before and after receiving ocrelizumab, including their weight in kilograms, age, gender, race, ethnicity, and MS subtype, duration, and disability (Expanded Disease Status Scale; EDSS). There was an average of 10.96 ± 5.76 months between the two weight measurements. Changes in weight were examined using a one-sample Wilcoxon signed rank test, while associations between weight changes and demographic and clinical variables were assessed with Spearman's rho (ρ) correlations and Mann-Whitney U tests.

Results: Over 52% of patients (n = 80) gained weight after receiving ocrelizumab (median: 2.36 kg), while nearly 39% (n = 59) lost weight (median: -1.90 kg). In the overall sample (n = 152), there was a significant change from pre-treatment weight ($z = 2.51$, $p = .012$), with a median change of 0.37 kg (range: -7.72 – 17.30 kg). Changes in weight were negatively correlated with EDSS scores ($\rho = -.18$, $p = .045$), with patients experiencing weight gain having a median EDSS score of 3 (range: 0 – 7.0) and patients experiencing weight loss having a median EDSS score of 4.0 (range: 1.5 – 7.5). There were no other significant associations.

Conclusions: Findings from this preliminary study suggest that weight changes post-ocrelizumab are frequently seen, with most patients either gaining weight or experiencing weight loss. As the EDSS score was the only variable associated with weight changes, further investigation is warranted to understand the underlying phenomenon, as well as the normal distribution of weight changes for persons with MS under more controlled time frames and across all levels of EDSS.

Disclosure: *Olivia Wei, Elizabeth S. Gromisch, Lindsay O. Neto, Jennifer A. Ruiz: Nothing to disclose. Peter Wade: Biogen, Celgene, EMD Serono, Genentech, Mallinckrodt, Novartis, Sanofi-Genzyme (speakers bureau).*

Keywords: Disease-modifying treatments in MS, weight changes

(DXT57)

FAST: Faster and Safe Administration of Tysabri

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Background: Natalizumab (Tysabri) has been FDA approved since 2004 and the incidence of infusion reactions is extremely low and has not increased over the 10 years of observational study done by Biogen. Patients sometimes complain of the burden of being infused monthly and being in the infusion center for 2 hours. In fact, many patients refuse the hour of observation after they are comfortable with infusions. Therefore, is it possible to reduce the amount of infusion time for Natalizumab safely.

Objectives: To determine if Natalizumab can safely be given over 30 minutes versus the standard 60 minute IV infusion

Methods: Observational Study of Patients in MS Center of Greater Orlando's Infusion Center who consented to be infused over 30 minutes. Patients who were recruited for study had been on Natalizumab for greater than 6 months.

Results: 22 of 25, 88% of patients did very well with no effect. The 3 persons who had effects were mild and did not require any additional treatment

Conclusions: Administering Natalizumab over 30 minutes is a reasonable and safe option for most patients. Further studies are suggested to ensure validity

Disclosure: *Nothing to disclose.*

Keywords: Disease-modifying treatments in MS, Tolerability

(DXT58)

Reduction of Risk of Secondary Progressive Multiple Sclerosis within Two Years of Treatment with Cladribine Tablets: An Analysis of the Clarity Study

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Background:
Cladribine Tablets (CT) 10mg, cumulative dose 3.5 mg/kg (CT3.5; N=433) over 2 years showed

efficacy vs placebo (PBO; N=437) in patients with relapsing multiple sclerosis in the CLARITY study.

Objectives:
Explore (*post hoc*) the relationship between baseline Expanded Disability Status Scale (EDSS) and risk of progression to secondary progressive multiple sclerosis (SPMS) or to EDSS ≥6.0 in CLARITY.

Methods:
As progression to SPMS was not recorded during the trial, a proxy composite definition was used: confirmed disability progression (CDP), CDP within the leading EDSS-defined functional score (FS), EDSS post-baseline ≥4.0, pyramidal FS ≥2, all conditions met for at least 3 months (mo) in the absence of a relapse. Patients progressing to EDSS ≥6.0 were defined by having ≥1 post-baseline EDSS ≥6.0 with 3 or 6 mo CDP. In this post-hoc analysis, odds ratios and corresponding confidence intervals (CI) are estimated by a logistic regression model with treatment and baseline EDSS (≤3.0 or ≥3.5) as fixed effects.

Results:
Overall, proxy SPMS progression was seen in 6.7% of CT3.5 patients vs 13.5% for PBO (odds ratio [OR] 0.46 [95% CI: 0.28, 0.76]; p=0.0024). In the baseline EDSS ≤3.0 subgroup (CT3.5 n=257; PBO n=235), proxy SPMS progression occurred in 3.5% vs 7.7% (CT3.5 vs PBO; OR 0.44 [95% CI: 0.19, 0.99]; p=0.0471). In the baseline EDSS ≥3.5 subgroup (CT3.5 n=148; PBO n=157), proxy SPMS progression occurred in 12.2% vs 22.4% (CT3.5 vs PBO; OR 0.48 [95% CI 0.26, 0.9]; p=0.0212). Similar effects have been observed for each proxy SPMS component vs PBO. Proportions of patients with at least one EDSS value ≥6.0 post-baseline were 6.4% vs 14.5% (CT3.5 vs PBO; OR 0.4 [95% CI 0.24, 0.66]; p=0.0004). Corresponding proportions for patients with 3mo CDP with EDSS ≥6.0 were 3.5% vs 8.0% (CT3.5 vs PBO; OR 0.42 [95% CI 0.22, 0.82]; p=0.0114) and for patients with 6mo CDP with EDSS ≥6.0 were 2.8% vs 5.8% (CT3.5 vs PBO; OR 0.48 [95% CI 0.22, 1.02]; p=0.0566). Subgroup analysis by baseline EDSS showed that in patients with baseline EDSS ≤3.0, 0.8% vs 4.3% had at least one EDSS ≥6.0 (CT3.5 vs PBO; OR 0.18 [95% CI 0.04, 0.81]; p=0.0262). In patients with baseline EDSS ≥3.5, the corresponding proportions were 16.2% vs 29.9% (CT3.5 vs PBO; OR 0.45 [95% CI 0.26, 0.79]; p=0.0051).

Conclusions:
The risks of progressing to SPMS (proxy) within 2 years of treatment, or experiencing EDSS ≥6.0, are significantly reduced with CT3.5 vs PBO, regardless of baseline EDSS (≤3.0 or ≥3.5).

Disclosure: *Patrick Vermersch: Almirall, Celgene, Novartis, Roche (consulting fee). Biogen, Merck KGaA, Sanofi-Genzyme, Teva (consulting fee, research support). Gavin Giovannoni: Abbvie, Actelion, Almirall, Atara Bio, Bayer Schering Pharma, FivePrime, GlaxoSmithKline, GW Pharma, Merck KGaA, Pfizer Inc, Protein Discovery Laboratories, Sanofi-Genzyme, Teva Pharmaceuticals Industries Ltd, UCB, Vertex Pharmaceuticals (consulting fee). Biogen Idec, Ironwood, Merck and Co, Novartis (consulting fee, unrelated research support). Per Soelberg-Sorensen: Biogen (advisory board, research support). Biogen Idec, Sanofi-Aventis (speakers bureau). Genzyme*

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Keywords: Disease-modifying treatments in MS

(DXT59)

The Clarity Study: Efficacy Outcomes Among Patients Who Received Disease-Modifying Drugs Prior to Treatment with Cladribine Tablets

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Background:
Cladribine tablets (CT) 10 mg, (cumulative dose 3.5 mg/kg [CT3.5] over 2 years) showed efficacy versus placebo in patients with relapsing-remitting multiple sclerosis (RRMS) in the pivotal Phase III CLARITY study. The CLARITY study included patients treated with 0–2 disease-modifying drugs (DMDs) prior to study entry (patients treated with >2 DMDs prior to study entry were excluded). A total of 433 patients were randomized to CT3.5 and 437 patients to placebo.

Objectives:
To report clinical outcomes and magnetic resonance imaging (MRI) lesion counts in the sub-group of patients from CLARITY who had used a DMD at any time prior to randomization.

Methods:
Post hoc analysis of efficacy, annualized relapse rate (ARR), relapse free rate, MRI activity, and time to 3-month and 6-month confirmed EDSS progression (CDP), were stratified by the cohort of patients who had received a prior DMD treatment before entering the CLARITY study. P-values less than 0.05 were considered nominally significant.

Results:
Of those patients who received prior DMD (interferon beta [IFN β]-1a, IFN β-1b, glatiramer acetate, or natalizumab), 110 were randomized to CT3.5 and 132 received placebo. Among patients with prior DMD use, CT3.5, compared to placebo, resulted in a nominally significant reduction in ARR (CT3.5, 0.22; placebo, 0.42; $P<0.005$), a higher relapse-free rate (CT3.5,

70.4%; placebo, 55.9%; P=0.0204), a numerically lower risk of 3-month (hazard ratio [HR]=0.64, p=0.1589) and 6 month (HR=0.62, P=0.2071) CDP, and reductions in the brain lesion counts (P<0.001 for each type of lesion).

Conclusions:
Among patients who were pre-treated with either IFN β-1a, IFN β-1b, glatiramer acetate, or natalizumab, efficacy outcomes were similar to those seen in the full CLARITY active RRMS population, wherein patients who received CT3.5 showed statistically significant improvements in efficacy outcomes compared to placebo.

Disclosure: *Patrick Vermersch: Almirall, Celgene, Novartis, Roche (consulting fee). Biogen, Merck KGaA, Sanofi-Genzyme, Teva (consulting fee, research support). Kottil Rammohan: Acorda, Biogen Idec, EMD Serono, Genzyme, Novartis, Roche/Genentech, Sanofi-Aventis, Teva Neurosciences (speakers bureau). Doris Damian, Gerard Harty, Schiffon L. Wong: EMD Serono, Inc. (a business of Merck KGaA, Darmstadt, Germany) (salary). Dominic Jack: Merck KGaA (salary).*

Keywords: Disease-modifying treatments in MS

(DXT60)

Correlations between Four Common Measures of Cognition in Patients with Secondary Progressive Multiple Sclerosis

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Background: Cognitive impairment is common in patients with secondary progressive multiple sclerosis (SPMS). The oral Symbol Digit Modalities Test (SDMT), Paced Auditory Serial Addition Test (PASAT) and Brief Visuospatial Memory Test Revised (BVMTR) were used to track cognition changes in the EXPAND study. This analysis evaluates whether these tests are redundant or complementary in progressive disease.

Objectives: Evaluate relationship between common cognitive tests in patients with SPMS and identify whether these tests provide unique insights on disease progression.

Methods: EXPAND was a 36 month, randomized, placebo-controlled trial of siponimod (Mayzent®) 2 mg/day in patients with SPMS. Cross-sectional, pairwise Pearson correlations (r) between SDMT, PASAT, and BVMTR total learning (-TL) and delayed recall (-DR) indices were calculated by treatment group and combined. Correlations were examined for baseline and change in scores from first post-baseline measurement to Month 24. Correlations were: strong (>0.6), intermediate (0.4-0.6) or weak (<0.4); $p<0.05$ indicates that correlations were statistically different to zero. Analyses for hypothesis generation; no adjustment for multiple comparisons.

Results: Data were analyzed for 1644 patients (siponimod, n=1098; placebo, n=546). In both treatment groups at baseline, strong correlations (0.89) were found between BVMTR-TL and BVMTR-DR; intermediate correlations (0.45-0.59) were observed between all other tests (all $p<0.0001$). For change from baseline to Month 24, strong correlations persisted between BVMTR-TL and BVMTR-DR (siponimod, 0.68; placebo, 0.72; both $p<0.0001$), but correlations were weak between all other tests with both treatments (0.05-0.17; $p>0.05$ in many cases).

Conclusions: Cognitive outcomes were correlated at baseline, confirming large overlap in variance for BVMTR indices and intermediate shared variance for other measures at a single time point. Weak correlations of change to Month 24 between SDMT, PASAT and BVMTR may suggest that each test tracks different aspects of cognitive decline and/or has different test characteristics when applied repeatedly in patients with SPMS.

Disclosure: *Ralph H B Benedict: Acorda, Mallinckrodt, NIH, NMSS (contracted research). Biogen (cme speaker fees , consulting fee, contracted research). Celgene, EMD Serono (cme speaker fees , consulting fee). Genentech, Genzyme, Novartis (consulting fee, contracted research). Psychological Assessment Resources, Inc. (royalty). Roche, Sanofi, Takeda, Verasci (consulting fee). Xiangyi Meng, Wendy Su: Novartis Pharmaceuticals Corporation (salary). Amit Bar-Or: Atara Biotherapeutics, Bayer, Bayhill Therapeutics, Berlex, Biogen Idec, BioMS, Celgene/Receptos, Diogenix, Eli Lilly, F Hoffman-La Roche, Genentech, GlaxoSmithKline, Guthy-Jackson/GGF, Immunic, Janssen/Actelion, MAPI, Medimmune, Merck/EMD Serono, Novartis, Ono Pharmacia, Roche/Genentech, Sanofi-Genzyme, Teva Neuroscience, Wyeth (consulting fee). Bruce A C Cree: Akili, Alexion, Atara, Biogen, EMD Serono, Novartis, TG Therapeutics (consulting fee). Robert J. Fox: Actelion, EMD Serono, Genentech, Teva (consulting fee). Biogen, Novartis (consulting fee, contracted research). Patrick Vermersch: Biogen, Celgene, Merck, Teva (consulting fee). La Revue des Microbiotes (personal fees for serving as an editor). Novartis, Roche, Sanofi-Genzyme (consulting fee, contracted research). Ludwig Kappos: Actelion, Alkermes, Allergan, Almirall, Bayer, Biogen, Celgene, CSL Behring, df-mp, European Union, EXCEMED, GeNeuro, Genzyme, Merck, Mitsubishi Tanabe Pharma, Novartis, Pfizer, Receptos/Celgene, Roche, Roche Research Foundations, Sanofi-Aventis, Santhera, Swiss Multiple Sclerosis Society, Swiss National Research Foundation, Teva, UCB Pharma, Vianex (contracted research). Neurostatus products (license fees).*

Keywords: Disease-modifying treatments in MS

(DXT61)

Injection-Related Reactions with Subcutaneous Administration of Ofatumumab in Relapsing Multiple Sclerosis: Pooled Analysis of the Phase 3 Asclepios I and II Trials

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Background:

Ofatumumab, the first fully human anti-CD20 monoclonal antibody, with a monthly 20 mg subcutaneous (s.c.) dosing regimen, demonstrated superior efficacy (reductions in clinical relapses by 51%–59%, disability worsening by 33%–34%, and gadolinium-enhancing lesions by 94%–98%) versus teriflunomide in the two Phase 3 ASCLEPIOS I/II relapsing multiple sclerosis (RMS) trials. Injection-related reactions (IRRs) were the most common adverse events (AEs) observed.

Objectives:

To characterize the risk of IRRs (systemic and local site reactions) observed with ofatumumab in RMS patients.

Methods:

In the pooled ASCLEPIOS I/II trials, patients were randomized (1:1) to receive s.c. ofatumumab 20 mg (n=946) (loading dose: Days 1, 7 and 14; maintenance dose: every 4 weeks from Week 4) or oral teriflunomide 14 mg once daily (n=936), for up to 30 months. Patients in the teriflunomide group received matching placebo injections. All patients received the first four injections at the clinic and subsequent injections at home. Premedication was recommended, but not mandatory. Both systemic (during and within 24 hours post injection) and local site IRRs (at any time) were reported.

Results:

In the ofatumumab group, 20.6% (n=195) of the patients, and 15.3% (n=143) in the teriflunomide group experienced ≥1 systemic IRR. Incidence of systemic IRRs with the first injection was 14.4% with ofatumumab versus 7.5% with teriflunomide. The incidence of systemic IRRs decreased with subsequent doses and was similar to the matching placebo

injections in the teriflunomide group. The majority of IRRs (99.8%) were Grade 1/2 in severity; Grade 3 IRRs were observed in two patients (0.2%) with ofatumumab at the first injection (one of which was reported as a serious AE) versus none with teriflunomide. One additional IRR (Grade 1) was also reported as a serious AE with ofatumumab. The serious IRRs (0.2%) were manageable and patients continued treatment with no recurrences. No life-threatening IRRs were reported during the study. The most frequent (≥2%) IRR symptoms observed with ofatumumab were fever, headache, myalgia, chills, and fatigue. Majority of local site IRRs were mild to moderate in severity and non-serious in nature; the most frequently reported symptoms (≥2%) included erythema, pain, itching, and swelling.

Conclusions:

Systemic and local IRRs with ofatumumab 20 mg s.c. were mostly mild to moderate in severity. Beyond the first injection, IRRs were no more frequent with ofatumumab versus matching placebo injections.

Disclosure: *Ratnakar Pingili, Cecile Kerloeguen, Ayan Das Gupta, Valentine Jehl, Dieter A. Haering, Krishnan Ramanathan, Martin Merschhemke: Novartis (salary). Amit Bar-Or: Atara Biotherapeutics, Biogen Idec, Celgene, EMD Serono, Genentech/Roche, GlaxoSmithKline, MAPI, MedImmune, Merck, Novartis, Receptos, Sanofi Genzyme (consulting fee, grant support, speakers bureau). Jeffrey A. Cohen: Adamas, Convelo, Mylan, Population Council (consulting fee). Multiple Sclerosis Journal (co-editor). Patricia K. Coyle: Accordant, Alexion, Bayer, Biogen Idec, Celgene, Genzyme/Sanofi, GlaxoSmithKline, Mylan, Serono, TG Therapeutics (consulting fee). Actelion, Alkermes, Corrona LLD, MedDay, NINDS, PCORI (contracted research). Genentech/Roche, Novartis (consulting fee, contracted research). Anne H. Cross: Academic CME (CE provider) (speaking and preparation of slides for cme talk). Biogen, Celgene, TG Therapeutics (consulting fee). EMD Serono (consulting fee, contracted research). Genentech/Roche (consulting fee, contracted research, speakers bureau). Novartis (consulting fee, fees for non-cme/ce services received directly from commercial interest or its agent, scientific advisory board for asclepios i and ii). Projects in Knowledge (CE provider) (preparation of educational manuscripts; activities). Rockpointe (Potomac Center for Medical Education) (CE provider) (speakers bureau). Stephen L. Hauser: Alector (scientific advisory board member (stock options received)). Annexon, Bionure, Molecular Stethoscope, Symbiotix (scientific advisory board member (stock options previously received)). F. Hoffmann-La Roche (travel support/reimbursement and writing support for anti-cd20 meetings and presentations). Neurona (board of trustees member (stock options previously received)). Novartis (travel support/reimbursement for anti-cd20 meetings and presentations). Ludwig Kappos: Actelion, Minoryx, Receptos, Santhera (consulting fee, steering committee; advisory board). Allergan, Allmirall, CSL Behring, Pfizer (support for educational activities). Bayer Health Care (consulting fee, speakers bureau, steering committee; advisory board; support for educational activities; licence fees for neurostatus products; grants). Biogen, Merck (consulting fee, steering committee; advisory board; support for educational activities; licence fees for neurostatus products; grants). Celgene, Genzyme (consulting fee, steering committee; advisory board; support for educational activities). INNO-Swiss, Roche research foundation (grants). Novartis, Roche (consulting fee, contracted research, speakers bureau, steering committee; advisory board; support for educational activities; licence fees for neurostatus products; grants). Sanofi (consulting fee, speakers bureau, steering committee; advisory board; support for educational activities). Teva (consulting fee, steering committee; advisory board; support for educational activities; licence fees for neurostatus products).*

Keywords: Disease-modifying treatments in MS, Immunology and MS, Injection-related reactions

(DXT62)

Real-World Treatment Patterns in Patients with Multiple Sclerosis Using Disease-Modifying Therapies

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Background: Numerous disease-modifying therapies (DMTs) have been approved for the treatment of multiple sclerosis (MS) in the past decade, and few studies have assessed patterns of use among all approved DMTs.

Objectives: This study characterized patterns of DMT use in patients with newly diagnosed MS.

Methods: Adults with newly diagnosed MS were identified from January 2007 to October 2017 using the IBM MarketScan Commercial and Medicare databases. Patients had at least 12 months of continuous enrollment prior to their initial MS diagnosis and 2 years of follow-up. Up to 3 DMT lines of therapy (LOTs) were reported during a follow-up of 2 to 10.5 years. Discontinuation or switch of therapy was assessed.

Results: Of 29,647 patients with at least 2 years of follow-up from MS diagnosis, 14,627 were treated with DMTs. Of these, 49% had 1 DMT LOT during follow-up, 25% had 2 LOTs, and 27% had 3 LOTs. Injectable (subcutaneous [SC] or intramuscular [IM]) DMTs, comprising glatiramer acetate (GA), interferon beta-1a (IFNb-1a) (SC and IM), interferon beta-1b (IFNb-1b), and peginterferon beta-1a (pegIFNb-1a), were used by 87% of patients as first LOT, 68% as second LOT, and 67% as third LOT. Oral DMTs, including dimethyl fumarate, fingolimod, and teriflunomide, were used by 11% of patients as first LOT, but increased to 30% of second and 32% of third LOTs. Natalizumab, the only infusion DMT in this analysis, was used by less than 3% as first, second, and third LOTs. The most common pattern after ending the first LOT was discontinuation from all DMTs (51%), while 17% switched DMTs and 26% restarted the same DMT treatment later. Long-term discontinuation increased to 56% of patients with a second LOT and 58% with a third LOT. Patients on GA and IFNb-1b had the highest rates of discontinuation (52% to 61% for each drug and each LOT) and restart (18% to 31% for each drug and each LOT). Patients on pegIFNb-1a had the highest rates of switching to another DMT, ranging from 20% to 29%. Those taking dimethyl fumarate and fingolimod at first LOT were least likely to switch treatments throughout all LOTs.

Conclusions: Over 2 to 10.5 years of follow-up, most MS patients discontinued or switched from their first-line DMT, regardless of DMT type. Injectable DMTs were the most commonly used DMTs over this study period, though the rate of oral DMT use increased in later lines of therapy.

Disclosure: *Robert J. Fox: Actelion, Biogen, Celgene, EMD Serono, Genentech, Immunic, Novartis, Sanofi, Teva, and TG Therapeutics (consulting fee). Actelion, Biogen, Immunic, and Novartis (advisory committee). Biogen and Novartis (clinical trial contract and research grant funding). Rina Mehta, Tim Pham: Bristol-Myers Squibb (employment). Julie Park, Kathleen Wilson, Machaon Bonafede: IBM Watson Health (employment).*

Keywords: Disease-modifying treatments in MS, Treatment Patterns

(DXT63)

Associations between Treatment Satisfaction, Medication Beliefs, and Adherence to Disease Modifying Therapies in Patients with Multiple Sclerosis Among Adult Saudis: A Tertiary Care Center Experience

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Background:

Multiple sclerosis (MS) considered as one of the most common Neuro-immune diseases that leads to major disabilities in an affected patient with a significant burden and consequences to patients and their families. Even though till these days there is no available cure for MS, however, the last two decades witnessed a promising future for MS treatments drugs precisely disease-modifying therapies (DMTs) to reduce MS relapse and delay disability.
Adherence to DMTs has a significant impact on treatment outcomes and is considered a critical factor in succeeding therapeutic success. Accordingly, the need to examine this issue in Saudi Arabia stands.

Objectives:

To identify the factors associated with adherence to DMTs medications among MS patients in Saudi Arabia.

To evaluate the relationship between treatment satisfaction, medication beliefs, and DMTs adherence, and other factors

Methods: A survey was conducted in 2019 in neurology clinics in King Fahad Medical City (KFMC) in Riyadh. Patients were sampled from the KFMC's Data Base with population size of 387 patients. The survey measured self-reported DMT adherence (doses taken divided by doses prescribed during previous 2-week period—adherence ≥0.80), DMT satisfaction using the Treatment Satisfaction Questionnaire for Medication version II, medication beliefs using the Beliefs About Medicines Questionnaire, and demographic and clinical covariates. Relationships between variables were examined using multivariate logistic regression.

Results: Final analyses included 239 usable surveys. Mean ± SD participant age was 35.07 ± 9.7 years. Most respondents were female (74.9%)), taking an injectable DMT (49%), and adherent to DMT (64.4%). Significant predictors of DMT adherence were DMT Experience (naive vs. experienced (odds ratio [OR], 3.722; 95% CI, 1.487 - 9.316; P = .005), DMT Rout (oral vs. injectable; OR, 0.974; 95% CI, 0.952 - 0.995; P = .017), and Global Satisfaction; OR, 0.950; 95% CI, 0.926 - 0.975; P = <0.001)

Conclusions: In patients with MS sampled from KFMC's Data Base, medication beliefs was not significantly associated with DMT adherence while the Global satisfaction was significantly associated with DMT adherence. Based on significant predictors, patients taking injectable DMTs, and patients with previous experience with another DMT(s) are at higher risk for no adherence. Future research is warranted to assess relationships between variables in more diverse MS populations.

Disclosure: *Rola F. Alarieh: King Fahad Medical City (ownership interest).*

Keywords: Adherence to therapy , Disease-modifying treatments in MS

(DXT64)

Evaluation of Rituximab Regimens and Outcomes in Neuromyelitis Optica Patients from a Single Academic Medical Center: A Retrospective Chart Review

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Background: Neuromyelitis optica (NMO) is a rare neurological disease often mistaken for multiple sclerosis that has limited treatment options and significant morbidity and mortality. Rituximab has been used for several years with demonstrated efficacy, but the optimal use of this agent in this patient population remains unknown. This has led to varying practices even within a single center. The current study aims to identify current practices and associated outcomes at an academic medical center without a standardized treatment protocol.

Objectives: The primary endpoint is time to relapse after first rituximab dose. Secondary endpoints include cumulative relapses, proportion of patients relapsing, and adverse event rate. This data will be used to work towards a standard protocol amongst NMO providers at the associated practice and will be hypothesis-generating for further research on the optimal use and place in therapy of rituximab for NMO/NMOSD in light of new and emerging treatment options

Methods: A retrospective chart review was conducted on approximately 60 patients at least 18 years old with NMO or NMO spectrum disorder who received at least 2 doses of rituximab and

were seen by a Penn Medicine neurology provider between February 1, 2013 and February 1, 2019. Patients were excluded due to a concurrent diagnosis of sarcoidosis, active cancer, or chronic infection (hepatitis B or C, TB, or HIV). Data collected includes: gender, age, weight/BMI, race, diagnosis, NMO episode/relapse history, aquaporin-4 antibody serostatus, prior treatment, dates and doses of rituximab, CD19+ B cell level and lab draw date, and adverse effects.

Results: Data will be analyzed with descriptive statistics

Conclusions: It is anticipated that we will identify a superior dosing strategy that will edify the practice of Rituxan dosing in NMO patients at our institution.

Disclosure: *Nothing to disclose.*

Keywords: TYPE NEW KEYDiseaseWORD HERE

(DXT65)

Longitudinal Disability Follow-up in Patients With 6-Month Confirmed Disability Improvement or Worsening in the CARE-MS and Extension Studies

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Background: In the 2-year CARE-MS trials (NCT00530348; NCT00548405), alemtuzumab (12 mg/day; baseline: 5 days; 12 months later: 3 days) significantly improved clinical/MRI outcomes versus subcutaneous interferon beta-1a in RRMS patients. Efficacy in alemtuzumab-treated patients was maintained through Year 9 in 2 consecutive extension studies (NCT00930553; NCT02255656 [TOPAZ]).

Objectives: To evaluate the status of disability over 9 years in pooled CARE-MS patients who had either 6-month confirmed disability improvement (CDI) or 6-month confirmed disability worsening (CDW) by Years 2 or 9.

Methods: Alemtuzumab-treated CARE-MS patients with baseline EDSS score ≥2 were stratified into 3 subgroups: with CDI, with CDW, or with stable disability. CDI and CDW were defined as ≥1-point decrease and increase, respectively, in EDSS score from core study baseline confirmed over 6 months. Improved and stable EDSS scores each year were defined as ≥1-point decrease and ≤0.5-point change in either direction, respectively, from core study baseline in available patients.

Results: 511/811 (63%) alemtuzumab-treated patients had baseline EDSS score ≥2. Of these, 222 (43%) patients had 365 unique CDI events and 172 (34%) patients had 217 CDW events at any time during the 9-year study; 31 (6%) had both CDI and CDW. Few patients (n=12) had a CDW event after CDI. Of patients with CDI at any time over 9 years, mean EDSS score change was –0.58 at Year 9 versus core study baseline, and 51% had lower EDSS scores at Year 9. Similar EDSS outcomes were observed at Year 9 in the subset of patients who achieved CDI within the first 2 years of the study. However, patients with CDW any time over 9 years had worsened disability at Year 9, with a +1.71 mean change in EDSS score from core study baseline; patients with CDW in the first 2 years of the study had a +2.27 EDSS change by Year 9. EDSS scores remained stable at 9 years (mean change, –0.10) in the 148 (29%) patients who had neither CDI nor CDW. Compared with previous years, no new safety signals were identified in Year 9 in CARE-MS extension study patients.

Conclusions: Achievement of CDI at any point in the CARE-MS studies was associated with improved disability at Year 9 versus baseline. However, those with CDW experienced increased disability over 9 years regardless of when worsening occurred. These findings suggest that both CDI and CDW are meaningful endpoints for predicting long-term disability outcomes in RRMS patients.

STUDY SUPPORT: Sanofi and Bayer HealthCare Pharmaceuticals

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Keywords: CNS repair, Disease-modifying treatments in MS

(DXT66)

Clinical Benefits of Eculizumab Monotherapy in Neuromyelitis Optica Spectrum Disorder: Findings from the Phase 3 Prevent Study

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Background: In the PREVENT study in patients with aquaporin-4 immunoglobulin G-positive (AQP4-IgG+) neuromyelitis optica spectrum disorder (NMOSD), eculizumab was associated with a significant reduction in relapse risk versus placebo and was well tolerated. The time course of relapses in prespecified subgroups suggested a treatment effect consistent with that in the overall population, regardless of use of permitted concomitant immunosuppressive therapy (IST) (rituximab and mitoxantrone were excluded).

Objectives: To examine the efficacy of eculizumab relative to placebo in patients with AQP4-IgG+ NMOSD who did not receive concomitant IST during the randomized, double-blind, placebo-controlled, phase 3 PREVENT trial (NCT01892345).

Methods: Adults with AQP4-IgG+ NMOSD received eculizumab (maintenance dose, 1200 mg/2 weeks, n = 96) or placebo (n = 47) with/without concomitant IST. A *post hoc* descriptive analysis of clinical outcomes was performed using data from patients who did not receive concomitant IST during PREVENT (ie eculizumab monotherapy or placebo without concomitant IST subgroup). Clinical outcomes comprised relapses, hospitalizations and acute treatment for relapses, and worsening of Expanded Disability Status Scale (EDSS) or Hauser Ambulation Index (HAI) scores.

Results: Of 34 patients in the no-IST subgroup: 10 had never received IST for NMOSD, 14 had previously received rituximab. Adjudicated relapses occurred in 0/21 patients receiving eculizumab monotherapy and 7/13 (53.8%) receiving placebo ($p < 0.0001$; *post hoc* analysis). In the placebo group, 6/13 patients (46.2%) were hospitalized for adjudicated relapses, 3 (23.1%) received plasma exchange, 4 (30.8%) were treated with acute intravenous methylprednisolone and 1 (7.7%) received high-dose oral corticosteroids. EDSS scores worsened in 1/21 patients (4.8%) receiving eculizumab monotherapy and 5/13 (38.5%) patients receiving placebo. HAI scores worsened in 1/21 patients (4.8%) receiving eculizumab monotherapy and 4/13 (30.8%) patients receiving placebo.

Conclusions: These data further characterize the substantial efficacy of eculizumab monotherapy in reducing relapse risk in patients with AQP4-IgG+ NMOSD. Patients receiving eculizumab monotherapy were spared relapse-associated hospitalizations and acute treatments, and the majority (95%) did not experience disability worsening. Long-term results from PREVENT's open-label extension will be presented.

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Keywords: Eculizumab Monotherapy in NMOSD

(DXT67)

Cognitive Functions over the Course of 5 Years in Multiple Sclerosis Patients Treated with Disease Modifying Therapies

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Background: Cognitive decline is common in multiple sclerosis (MS). Disease-modifying therapies (DMTs) are applied to delay or prevent disease progression in MS. While this has mostly been proven for physical status, comprehensive data on cognitive functions are not yet available.
Objectives: We aimed to present 5 years of cognition data of patients treated with DMTs.

Methods: In totally, 756 patients with MS who were treated with interferon beta (1b or 1a, SC) (n=342), glatiramer acetate (GA) (n=188) or fingolimod (n=226). Mean age was higher in fingolimod group ($p< 0.05$). Physical disability was assessed with expanded disability status scale (EDSS) and cognitive status was assessed with Brief International Cognitive Assessment for MS (BICAMS) which included the Symbol Digit Modalities Test (SDMT), the California Verbal Learning Test-II (CVLT-II) and the Brief Visuospatial Memory Test-Revised (BVMT-R). Assessments were performed at baseline and yearly till the end fifth year of treatment.

Results: 85% of patients treated with fingolimod were still having their madicaton at the end of fifth year (79% for GA, and 78.9% for interferon beta, $p< 0.05$).

Most of the patients treated with DMTs remained stable over the course of 5 years (fingolimod: 70,1%, interferons: 71.9%, GA: 75%, $p>0.05$). Cognition improved in some patient (fingolimod: 11.2%, interferons: 9.6%, GA: 8%, $p>0.05$). More than 80% of patients remained stable or improved. The most significant improvement was observed in SDMT, and it was significantly higher than CVLT-II, and BVMT-R (30.7%, 18.6%, 17%, respectively, $p=0.02$)

Conclusions: In conclusion, cognitive functions remain stable under DMTs over 5 years. This condition has not shown a relationship with the type of madication. Furthermore, SDMT seems to be the best predictor for cognitive change in time.

Disclosure: *Nothing to disclose.*

Keywords: Disease-modifying treatments in MS, Psychological issues and MS

(DXT69)

One-Year Interim Analysis of Real-World Patient-Reported Outcomes in RRMS Patients Transitioning to Alemtuzumab (PRO-ACT Study)

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Background: Clinical trials of alemtuzumab have demonstrated its 9-year efficacy and safety, but real-world data are limited. PRO-ACT assesses patient-reported outcomes (PROs), safety, and treatment sequencing in adults with RRMS transitioning from prior disease-modifying therapy to alemtuzumab in the United States and Canada.

Objectives: To report the 1-year interim results of the real-world PRO-ACT study.

Methods: PRO-ACT is an ongoing 24-month, prospective, multicenter, noninterventional, single-arm, observational study. The primary endpoint evaluates change in overall satisfaction on the Treatment Satisfaction Questionnaire for Medication v1.4 (TSQM; scale 0−100; higher scores indicate greater satisfaction), after transitioning to alemtuzumab. Other PROs evaluated (lower scores indicate improved outcomes) are the MS Impact Scale-29 (MSIS-29; scale 0−100), Modified Fatigue Impact Scale-5 (MFIS-5; scale 0−20), Patient-Determined Disease Steps (PDDS; scale 0−8), and Health-Related Productivity Questionnaire (HRPQ)-MS v2.

Results: As of September 2019, enrollment was complete (N=200 patients) and PRO data were evaluable in 170 patients. Patients transitioned from natalizumab (37%), dimethyl fumarate (14%), fingolimod (13%), teriflunomide (12%), or other therapies (24%) to alemtuzumab. Mean TSQM scores improved from baseline to Year (Y) 1 for overall satisfaction (50.3 vs 66.5; $P<0.0001$) and effectiveness (49.3 vs 60.7; $P<0.0001$) domains; scores were unchanged for side effects (77.6 vs 76.5) and convenience (70.3 vs 70.7). Mean scores for other PROs showed improvement at Y1 versus baseline: MSIS-29 physical impact scale (52.4 vs 47.8; $P<0.001$), MSIS-29 psychological impact scale (53.4 vs 47.9; $P<0.001$), and MFIS-5 (12.8 vs 11.7; $P<0.001$). Scores remained stable on the PDDS (3.1 vs 3.2). Mean hours of weekly employment productivity lost decreased from 11.4 at baseline to 7.4 at Y1 ($P<0.05$). Incidence of adverse events was 92% and serious adverse events was 11%. One death occurred (suicide).

Conclusions: PROs improved during the first year of alemtuzumab treatment after transitioning from another therapy. Alemtuzumab safety in Y1 was consistent with the pivotal studies.

STUDY SUPPORT: Sanofi

Disclosure: *Sibyl Wray: Alkermes, Biogen, Celgene, Genentech, Novartis, Sanofi, TG Therapeutics (consulting, principal investigator, and/or speaking fees). Francois Jacques: Biogen, Merck Serono, Novartis, Roche, Sanofi (honoraria for giving presentations, advisory board participation, research funding, and for an infusion clinic).*

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Keywords: Disease-modifying treatments in MS

(DXT70)

Clinical Characteristics and Outcomes of Peginterferon Beta-1a Treatment By Age: A Subgroup Analysis of the Plegridy Observational Program

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Background: Peginterferon beta-1a is approved to treat relapsing forms of multiple sclerosis (RMS) based on results from the ADVANCE trial, which had a mean patient age of 36 years. US claims data show a mean age in the peginterferon beta-1a patient postmarketing population of 45-50 years, yet data on disease-modifying therapies for patients aged ≥50 with RMS are limited. The 5-year, Phase 4 Plegridy Observational Program (POP) study explores the real-world safety and effectiveness of peginterferon beta-1a in patients with RMS, a third of whom are aged ≥50.

Objectives: Report on baseline (BL) characteristics, safety outcomes, and clinical effectiveness of peginterferon beta-1a in patients ≥50 and <50 years of age enrolled in POP.

Methods: The safety analysis population included 1126 patients; 375 (33%) were ≥50 and 751 (67%) were <50 years of age at BL. The effectiveness analysis population included 1125 (≥50, 375; <50, 750) patients. Data reflect the third interim data cut as of September 2018. Data from the fourth interim data cut (September 2019) will be presented.

Results: The mean (standard deviation) age of ≥50 and <50 patients was 58.0 (6.2) and 36.8 (8.2) years at BL, respectively, and 45.2 (9.4) and 31.7 (7.6) years at MS diagnosis, respectively. The percentage of female patients was similar in the ≥50 (74.7%) and <50 (77.1%) subgroups. At BL, the mean time since MS symptom onset was higher for the ≥50 group than the <50 group (17.1 years vs. 7.4 years). Patients ≥50 had fewer relapses in the year prior to BL (mean: 0.3 vs. 0.6) and in the 3 years prior to BL (mean: 0.6 vs. 1.0) than patients <50. At BL, the mean Expanded Disability Status Scale score was higher in patients ≥50 (2.69) vs. patients <50 (1.45). The incidence of treatment-emergent adverse events (AEs) in POP was similar in the ≥50 (63.2%) and <50 (62.7%) subgroups. A higher incidence of serious AEs (SAEs) was reported in patients ≥50 (9.6%) vs. <50 (5.1%). The annualized relapse rate (ARR) was 0.08 in patients ≥50

and 0.15 in those <50. The percent of relapse-free patients over 3 years was 88.3% in patients ≥50 and 78.3% in patients <50.

Conclusions: In both subgroups, the incidence of AEs was similar; the incidence of SAEs was higher in patients aged ≥50. ARR was low and the percentage of relapse-free patients was high in both subgroups, indicating that peginterferon beta-1a has the potential to provide treatment benefits to patients with RMS, including those aged ≥50.

Support: Biogen

Disclosure: *Sibyl Wray: Bayer, Biogen, Celgene, EMD Serono, Genentech/Roche, Genzyme/Sanofi, Novartis, Receptos, TG Therapeutics (paid consultant, speaker, and/or contract researcher). Marco Salvetti: Biogen, Merck, Novartis, Roche, Sanofi, Teva (received grant support and/or speaker honoraria). Gereon Nelles: Bayer, Biogen, Celgene, Merck, Novartis, Roche (received speaker honoraria). Arman Altincatal, Megan C. Vignos, Achint Kumar, Maria L. Naylor: Biogen (employee of, and may hold stock and/or stock options in, biogen).*

Keywords: age, Disease-modifying treatments in MS

(DXT71)

Efficacy and Safety of Teriflunomide in Patients With RRMS of Varying Disease Duration: Analysis of Pooled Clinical Trials

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Background: Teriflunomide is a once-daily oral immunomodulator approved for the treatment of relapsing forms of MS or RRMS, depending on the local label.

Objectives: To assess the long-term efficacy and safety of teriflunomide in patients with RRMS stratified by disease duration.

Methods: This was a pooled efficacy and safety analysis using data from the phase 2 study (NCT01487096), and the phase 3 TEMSO (NCT00134563, NCT00803049), TOWER

(NCT00751881), and TENERE (NCT00883337) core and extension studies. Patients receiving placebo or teriflunomide 14 mg were stratified by disease duration at baseline (≤1 year, >1 to ≤5 years, >5 to ≤10 years, and >10 years). Study endpoints included annualized relapse rate (ARR), EDSS score, 6-month confirmed disability worsening (CDW), and safety.

Results: In the core period, ARR was lower in patients treated with teriflunomide 14 mg compared with placebo across disease duration subgroups: ≤1 year (0.33 [n=272] vs 0.56 [n=251], *P*=0.0013), >1 to ≤5 years (0.46 [n=278] vs 0.70 [n=268], *P*=0.0011), >5 to ≤10 years (0.39 [n=191] vs 0.52 [n=164], *P*=0.0571), and >10 years (0.33 [n=154] vs 0.58 [n=129], *P*=0.0005). In the core+extension period (up to Year 13), ARRs in teriflunomide-treated patients were similar regardless of disease duration: ≤1 year (0.19; n=276), >1 to ≤5 years (0.22; n=699), >5 to ≤10 years (0.26; n=393), and >10 years (0.25; n=325). At Year 13, 6-month CDW rates for each group were 48.3% (≤1 year), 37.1% (>1 to ≤5 years), 52.6% (>5 to ≤10 years), and 36.8% (>10 years). From core study baseline to Year 10 (the last time point at which all groups had at least 10 patients), EDSS scores were stable across teriflunomide-treated patients of different disease duration: ≤1 year, +0.27; >1 to ≤5 years, +1.11; >5 to ≤10 years, +0.05; and >10 years, +0.7. Overall incidences of adverse events (AEs) through Year 13 were 93.1% (≤1 year), 87.2% (>1 to ≤5 years), 88.0% (>5 to ≤10 years), and 88.7% (>10 years); incidences of serious AEs during this period were 21.2% (≤1 year), 19.1% (>1 to ≤5 years), 15.5% (>5 to ≤10 years), and 18.0% (>10 years).

Conclusions: Teriflunomide 14 mg reduced relapses across all patients regardless of disease duration versus placebo in the core studies. Over 13 years, ARR remained low and EDSS increased minimally. Safety outcomes from baseline to Year 13 were consistent across disease duration subgroups.

STUDY SUPPORT: Sanofi

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Keywords: Disease duration and age in MS, Disease-modifying treatments in MS, Natural history of MS

(DXT73)

Updated Safety of Cladribine Tablets in the Treatment of Patients with Multiple Sclerosis: Integrated Safety Analysis and Post-Approval Data

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Background:
Pooling of long-term safety data for integrated analysis from the clinical trial program allows comprehensive characterization of the cladribine tablets (CT) 10 mg (3.5 mg/kg cumulative dose over 2 years [CT3.5]) safety profile in patients with relapsing multiple sclerosis (RMS).

Objectives:
To provide an update to the previously reported treatment-emergent adverse event (TEAE) profile for CT using the latest integrated safety data from clinical studies, including final data from the PREMIERE registry, and report post-approval safety data from Europe.

Methods:
The monotherapy oral cohort (CT3.5, N=923, patient-years [PY]=3936.69; placebo [PBO], N=641, PY=2421.47) was derived from the CLARITY, CLARITY Extension, and ORACLE MS trials, and the PREMIERE registry. Incidences per 100PY were calculated for adverse events, cumulative to the end of PREMIERE. Adverse drug reactions (ADRs) including serious ADRs (SADRs; implied causality) from post-approval sources are summarized.

Results:
Demographics reported at first dosing date were balanced among treatment groups: mean age (CT3.5=37.8 years; PBO=37.2 years); proportion of females (CT3.5=66.3%; PBO=66.1%); and proportion of patients with prior disease modifying drug experience (CT3.5=19.9%; PBO=20.4%). Incidences per 100PY for experiencing ≥1 serious TEAE were 3.80 (CT3.5) and 3.05 (PBO). Incidences per 100PY for serious lymphopenia (preferred term [PT]) were 0.10 for CT3.5 and 0 for PBO. For serious infections and infestations (system organ class), incidences per 100PY were 0.60 (CT3.5) and 0.42 (PBO); for serious herpes zoster (PT): 0.05 (CT3.5) and 0

(PBO). Incidences per 100PY for malignant tumors were 0.26 (CT 3.5) and 0.12 (PBO). Separately, 922 ADRs from post-approval sources were reported in the Periodic Benefit-Risk Evaluation Report, of which 136 were SADRs; none of which are new safety findings for CT3.5.

Conclusions:
This integrated analysis of trial data, exclusively focused on the frequency of serious TEAEs with CT3.5 in RMS patients, further establishes the safety profile of this dose. This profile is consistent with the previously published integrated safety analysis profile. No new major safety findings were identified in this latest dataset which includes final data from the PREMIERE registry. The pattern of post-approval ADRs was consistent with the clinical safety profile for CT3.5.

Disclosure: *Stuart Cook: Actinobac Biomed Inc, Biogen Idec, Merck KGaA, Teva Pharmaceuticals (advisory board). Bayer Healthcare (advisory board, grant support). Neurology Reviews, Sanofi Aventis (consulting fee). Gavin Giovannoni: Abbvie, Actelion, Almirall, Atara Bio, Bayer Schering Pharma, FivePrime, GlaxoSmithKline, GW Pharma, Merck KGaA, Pfizer Inc, Protein Discovery Laboratories, Sanofi-Genzyme, Teva Pharmaceuticals Industries Ltd, UCB, Vertex Pharmaceuticals (consulting fee). Biogen Idec, Ironwood, Merck and Co, Novartis (consulting fee, unrelated research support). Thomas P. Leist: Acorda, Bayer, Biogen, Daiichi, EMD Serono, Novartis, ONO, Pfizer, Teva Neuroscience (consulting fee). Giancarlo Comi: Almirall SpA, Biogen Idec, Biogen Italia Srl, Celgene Group, Excemed, F. Hoffman-La Roche, Forward Pharma, Genzyme Corporation, Genzyme Europe, Medday, Merck KGaA, Merck Serono SpA, Novartis, Roche SpA, Sanofi Genzyme, Teva Italia Srl, Teva Pharmaceutical Industries Ltd. (consulting fee). Sana Syed, Doris Damian: EMD Serono, Inc. (a business of Merck KGaA, Darmstadt, Germany) (salary). Axel Nolting, Regina Schick: Merck KGaA (salary).*

Keywords: Disease-modifying treatments in MS

(DXT74)

An Analysis of the Relationship between Cladribine Dose and Risk of Malignancies in Patients with Multiple Sclerosis

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Background:
Malignancy risk was previously characterized in a Monotherapy Oral cohort of patients with multiple sclerosis (MS) treated with cladribine tablets (CT) 10 mg (3.5 mg/kg cumulative dose over 2 years; referred to as CT3.5) including cumulative data up to Feb 2015. In clinical studies,

an imbalance in the number of malignancies with CT3.5 vs placebo (PBO) was observed, suggesting malignancy risk may be increased.

Objectives:
To provide a more detailed assessment of malignancy using safety data integrated from clinical trials and a safety follow-up registry (up to May 2017), to further characterize the malignancy risk of CT in patients with MS and investigate whether there is a dose-dependent risk.

Methods:
Cohorts were Monotherapy Oral: patients with MS receiving CT at any dose as a monotherapy; All Exposed: patients with MS receiving any formulation of cladribine to provide a larger cohort to identify rare events such as malignancies.

Results:
In the Monotherapy Oral cohort, patient numbers (patient-years [PY]) were: PBO N=641 (2275), CT3.5 N=923 (3754), CT 5.25 mg/kg (CT5.25) N=632 (2610). The incidence per 100PY for malignant tumors during the entire follow up was: PBO: 0.13, CT3.5: 0.27, and CT5.25: 0.23. The risk difference vs PBO was: CT3.5: 0.14 (95% confidence interval [CI] -0.14–0.38) and CT5.25: 0.10 (-0.18–0.39). In CLARITY CT3.5 and CT5.25 patients randomized to CT3.5 in CLARITY Extension (N=195 for each treatment group), incidence per 100PY by CLARITY CT dose was: 0.55 (CT3.5, 1301PY) and 0.31 (CT5.25, 1286PY) for the entire follow-up; 0.91 (CT3.5, 790PY) and 0.52 (CT5.25, 784PY) for the period following initiation of treatment in Year 3. An analysis of the All Exposed cohort (cladribine N=1976; PBO N=802) stratified by cumulative cladribine dose gave the number of patients with a malignant event (incidence per 100PY) as: >0–3.5 mg/kg = 6 (0.37), >3.5–5.25 = 14 (0.40), >5.25–7.0 = 6 (0.29), >7.0–8.75 = 6 (0.46), >8.75 = 2 (0.21). No hematological malignancies were observed at any time in the pooled dataset.

Conclusions:
Overall, there was no clear evidence of a dose effect of cladribine on malignancy risk in patients with MS based on >9500PY of cladribine exposure.

Disclosure: *Stuart Cook: Actinobac Biomed Inc, Biogen Idec, Merck KGaA, Teva Pharmaceuticals (advisory board). Bayer Healthcare (advisory board, grant support). Neurology Reviews, Sanofi Aventis (consulting fee). Gavin Giovannoni: Abbvie, Actelion, Almirall, Atara Bio, Bayer Schering Pharma, FivePrime, GlaxoSmithKline, GW Pharma, Merck KGaA, Pfizer Inc, Protein Discovery Laboratories, Sanofi-Genzyme, Teva Pharmaceuticals Industries Ltd, UCB, Vertex Pharmaceuticals (consulting fee). Biogen Idec, Ironwood, Merck and Co, Novartis (consulting fee, unrelated research support). Thomas P. Leist: Acorda, Bayer, Biogen, Daiichi, EMD Serono, Novartis, ONO, Pfizer, Teva Neuroscience (consulting fee). Giancarlo Comi: Almirall SpA, Biogen Idec, Biogen Italia Srl, Celgene Group, Excemed, F. Hoffman-La Roche, Forward Pharma, Genzyme Corporation, Genzyme Europe, Medday, Merck KGaA, Merck Serono SpA, Novartis, Roche SpA, Sanofi Genzyme, Teva Italia Srl, Teva Pharmaceutical Industries Ltd. (consulting fee). Axel Nolting, Elke Sylvester, Dominic Jack: Merck KGaA (salary). Doris Damian: EMD Serono, Inc. (a business of Merck KGaA, Darmstadt, Germany) (salary). Andrew Galazka: Merck KGaA, Aubonne, Switzerland (a business of Merck KGaA, Darmstadt, Germany) (salary).*

Keywords: Disease-modifying treatments in MS

(DXT75)

Switches to Established and Recently Approved Oral Disease-Modifying Therapies: Comparison of Patient Clinical Profiles and Therapy Selection Drivers

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Background: With the approval of siponimod (BAF), cladribine (CdA), and diroximel fumarate (DRF) in the United States, the number of oral disease-modifying therapies (DMTs) for the treatment of multiple sclerosis (MS) has grown.

Objectives: To compare clinical profile, treatment history, and switch drivers among MS patients recently switched to an oral DMT.

Methods: In February 2019, 209 U.S. neurologists contributed to a cross-sectional, retrospective chart audit of MS patients [n=1,003 total; n=718 relapsing-remitting MS (RRMS)] switched to a new DMT no more than three months prior. Patients were characterized by likelihood of alternative switch to DMTs in development, if the therapies had been available at switch. Analyses will be updated with February 2020 data.

Results: The majority of patients recently switched to an oral DMT were diagnosed with RRMS (87%-92%). Oral DMTs constituted 43% of RRMS switches, with 11% switched to teriflunomide (TLF), 16% to fingolimod (FTY), and 17% to dimethyl fumarate (DMF). Oral RRMS switches were predominantly first switches (85%-89%); such switches were frequently due to efficacy (39%-43%) or tolerability (25%-29%). Patients switched to FTY were more likely to have switched from another oral DMT compared to those switched to DMF (21% vs. 7%, $p<0.05$). Desire for a high-efficacy DMT drove more FTY switch selection (60% vs. TLF: 32%, DMF: 35%; $p<0.05$), whereas patient request (30% vs. FTY: 15%; $p<0.05$) and lack of monitoring (16% vs. FTY: 2%; $p<0.05$) were more influential in DMF switches and long-term safety in TLF switches (39% vs. FTY: 20%; $p<0.05$). Compared to the established oral DMTs, candidates for alternative BAF, CdA, or DRF switches were less likely to be diagnosed with RRMS and more likely to have experienced a second or later switch. RRMS patients considered CdA candidates were more likely to have switched from an oral DMT compared to noncandidates (22% vs. 12%; $p<0.05$); administration type preference (43% vs. 26%; $p<0.05$), good tolerability profile (49% vs. 38%; $p<0.05$), and long-term safety (34% vs. 22%; $p<0.05$) drove more of the switched-to DMT selections among CdA candidates. DRF candidates were more likely to have switched due to tolerability issues compared to noncandidates (34% vs. 16%; $p<0.05$).

Conclusions: Switches to established oral DMTs are typically first switches among RRMS patients, although FTY may be reserved as a high-efficacy option for patients who have failed a prior oral DMT. Oral class impact will grow within the switch segment with the availability of new oral options; however, the recently approved therapies will initially be niched as later line options. 2020 chart audit data will assess early adoption patterns and selection drivers among patients switched to BAF, CdA, or DRF.

Disclosure: *Nothing to disclose.*

Keywords: Disease-modifying treatments in MS

(DXT76)

First-Line Ocrelizumab Use for Relapsing-Remitting Multiple Sclerosis in the United States: Trend and Comparison to Glatiramer Acetate and Dimethyl Fumarate

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Background: In March 2017, ocrelizumab (OCR) was approved for the treatment of relapsing-remitting and primary progressive multiple sclerosis (MS), irrespective of prior therapy exposure. The relapsing-remitting MS (RRMS) indication was updated in July 2019 to encompass all relapsing forms of MS, including clinically isolated syndrome, RRMS, and active secondary progressive MS.

Objectives: To trend OCR uptake among previously treatment-naïve RRMS patients and compare characteristics of RRMS patients initiated on first-line OCR to those initiated on one of the more established platform disease-modifying therapies (DMTs), glatiramer acetate (GA) or dimethyl fumarate (DMF).

Methods: A retrospective, cross-sectional chart audit of MS patients who initiated their first DMT no more than three months prior (i.e., new start patients) has been conducted with U.S. neurologist (2016 n=242; 2017 n=274; 2018 n=213) each December. Data were based on contributed RRMS patient chart reviews (2016 n=777; 2017 n=801; 2018 n=758). GA includes patients treated with either a branded or generic agent. December 2019 data will be included at presentation.

Results: In 2018, OCR was prescribed to 5%, GA to 32%, and DMF to 19% of new start RRMS patients — stable with prior years. Although neurologists are more likely to agree with being comfortable using Ocrevus first line for RMS patients (57% vs. 38% in 2017; $p<.05$), statement agreement did not correlate significantly with OCR share. While OCR patients were more likely

to be male (OCR: 43%, GA: 24%, DMF: 26%), mean age or age category allocation did not differ between subgroups. RRMS patients initiated on OCR were more likely to have a perceived unfavorable long-term prognosis (OCR: 49%, GA: 11%, DMF: 8%) and to be experiencing disability progression (OCR: 24%, GA: 11%, DMF: 9%). In comparison, GA and DMF patients were more likely to have no symptoms per the modified Rankin Scale (OCR: 5%, GA: 29%, DMF: 33%). OCR patients had a greater mean T2 lesion burden at the most recent MRI scan (OCR: 6.9, GA: 4.3, DMF: 4.1) and, since first under the contributing neurologist's care, were more likely to have had a Gd-enhancing lesion(s) (OCR: 38%, GA: 11%, DMF: 7%), relapse(s) (OCR: 48%, GA: 22%, DMF: 21%), decreased walking speed (OCR: 38%, GA: 8%, DMF: 12%), and/or onset or progression of cognitive symptoms (OCR: 19%, GA: 5%, DMF: 2%). High efficacy desire, dosing schedule preference, peer recommendation, and patient nonadherence concern played significantly more of a role in the first-line selection of OCR compared to GA or DMF.

Conclusions: Regardless of neurologists' perceived comfort with first-line OCR, use among new start RRMS patients has remained flat during the first two years of availability. Compared to platform DMTs, OCR is most likely to be selected when a high efficacy agent is required due to risk factors suggesting a poor long-term prognosis at the time of DMT treatment initiation.

Disclosure: *Nothing to disclose.*

Keywords: Disease-modifying treatments in MS

(DXT77)

Alemtuzumab Maintains Efficacy on Clinical and MRI Lesion Outcomes, Including Slowing of Brain Volume Loss, Over 9 Years in RRMS Patients: CARE-MS II Follow-up (TOPAZ Study)

Barry A Singer[1] Raed Alroughani[2] Ann D Bass[3] Simon Broadley[4] Yang Mao-Draayer[5] Hans-Peter Hartung[6] Eva Kubala Havrdova[7] Ho Jin Kim[8] Kunio Nakamura[9] Carlos Navas[10] Alex Rovira[11] Krzysztof Selmaj[12] Patrick Vermersch[13] Sibyl Wray[14] Zia Choudhry[15] Nadia Daizadeh[15] Salman Afsar[15] Giancarlo Comi[16] on behalf of the CARE-MS II, CAMMS03409, and TOPAZ Investigators
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Background: In CARE-MS II (NCT00548405), alemtuzumab (12 mg/day; baseline: 5 days; 12 months later: 3 days) significantly improved clinical/MRI outcomes versus subcutaneous interferon beta-1a (SC IFNB-1a) over 2 years (y) in RRMS patients with inadequate response to prior therapy. Efficacy was maintained in a 4-y extension study (NCT00930553), wherein patients could receive additional alemtuzumab courses (12 mg/day on 3 days, ≥12 months apart) as needed for disease activity, or receive other disease-modifying therapy (DMT) per investigator discretion. Further follow-up was available in an additional 5-y extension, TOPAZ (NCT02255656).

Objectives: Evaluate the efficacy and safety of alemtuzumab in CARE-MS II patients over 9 y.

Methods: At investigator discretion, patients in TOPAZ can receive additional as-needed alemtuzumab (≥12 months apart, no criteria) or receive other DMT (at any time).

Results: From core study baseline through Y9, 288/435 (66%) CARE-MS II alemtuzumab-treated patients remained on study; 41% received neither additional alemtuzumab nor another DMT through Y9. Annualized relapse rate was 0.19 in Y3–9. From core study baseline through Y9, 68% of patients had stable/improved EDSS scores, and mean change in EDSS was +0.32. Over 9 y, 60% of patients were free of 6-month confirmed disability worsening and 49% achieved 6-month confirmed disability improvement. On average, 69% of patients were free of MRI disease activity, 89% were free of new gadolinium-enhancing lesions, and 69% were free of new/enlarging T2 hyperintense lesions, annually from Y3–9. From core study baseline through Y9, median percent cumulative brain volume (BV) change was –1.22%; median percent BV change was ≤–0.19% annually over Y3–9. Incidence of overall adverse events (AEs) and infections declined through Y9; cumulative thyroid AE incidence was 43.7% and immune thrombocytopenia (ITP) incidence was 3.7% (1 new case of ITP, 14 months after the fourth alemtuzumab course, was observed at Y9). No new cases of nephropathy were reported. Efficacy and safety in SC IFNB-1a−treated patients from the core study who switched to alemtuzumab in the extension were consistent with those treated with alemtuzumab both in the core and extension.

Conclusions: Efficacy of alemtuzumab on clinical, MRI, and BV loss outcomes was maintained over 9 y in CARE-MS II patients, with 41% receiving no further treatment through Y9. Safety in Y9 in this study was consistent with that of previous years.

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Keywords: Disease-modifying treatments in MS

(DXT78)

The Fluent Study: Changes in Immune Cell Profile, and in Clinical and Safety Outcomes in Fingolimod-Treated Patients with Relapsing Multiple Sclerosis

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Background: Fingolimod inhibits sphingosine 1-phosphate receptor-mediated lymphocyte egress from lymph nodes, reducing lymphocytic infiltration of the central nervous system in multiple sclerosis (MS). However, characterization of immune cell changes in relation to patient outcomes in MS remains incomplete.

Objectives: The FLUENT study explored fingolimod-mediated immune-cell subset changes in the innate and adaptive immune systems and their association with efficacy and safety outcomes in relapsing MS.

Methods: FLUENT was a 12-month, prospective, multicenter, nonrandomized phase IV study in adults with relapsing MS receiving fingolimod 0.5 mg/day (NCT03257358). Patients were stratified as fingolimod-naive (Cohort 1) or previously treated with fingolimod for ≥2 years (Cohort 2). The primary outcome was change from Baseline in immune cell subsets. Secondary outcomes included anti-John Cunningham virus (JCV) antibody status, neurofilament light-chain (NfL) concentrations, Patient-Determined Disease Steps (PDDS) and incidence of adverse events (AEs). Analyses were in patients completing Month 12 follow-up.

Results: At Baseline, proportions of CD4+ T cells, CD8+ T cells and B cells were higher in Cohort 1 (n=163) than in Cohort 2 (n=217). Cell counts in these immune subsets were substantially reduced at Month 12 compared with Baseline in Cohort 1, with naive and central memory T cells affected more than effector memory T cells and regulatory B cells; changes in these subsets were less pronounced in Cohort 2 than in Cohort 1. At Baseline, 54% of Cohort 1 and 64% of Cohort 2 were anti-JCV positive, and anti-JCV antibody index was unchanged at Month 12. Mean (standard deviation) NfL concentration in Cohort 1 was 12.16 (11.05) pgmL at Baseline and 8.57 (5.32) at Month 12; Nfl concentrations in Cohort 2 were similar at Baseline (9.59 [7.55]) and Month 12 (9.78 [8.88]). Baseline PDDS scores were low (Cohort 1, 1.7; Cohort 2, 1.8) and unchanged at Month 12. Respective rates of treatment-emergent AEs (54.6% vs 44.2%) and AEs leading to treatment discontinuation (12.3% vs 5.5%) were higher in Cohort 1 than Cohort 2; rates of serious AEs (5.5% vs 5.5%) were similar between cohorts.

Conclusions: These findings expand understanding of temporal changes in immune cell subtype profiles and biomarkers in patients with relapsing MS receiving fingolimod.

Disclosure: *Yang Mao-Draayer: Acorda, Bayer, Biogen, Celgene, EMD Serono, Genentech, Teva (consulting fee). Chugai, Novartis, Sanofi-Genzyme (consulting fee, contracted research). NIAID Autoimmune Center of Excellence, NIH NINDS (contracted research). Jeffrey A. Cohen: Convelo, Population Council (consulting fee). Multiple Sclerosis Journal (serving as editor). Mylan (speakers bureau). Amit Bar-Or: Atara Biotherapeutics, Bayer, Bayhill Therapeutics, Berlex, Biogen Idec, BioMS, Celgene/Receptos, Diogenix, Eli Lilly, F Hoffman-La Roche, Genentech, GlaxoSmithKline, Guthy-Jackson/GGF, Immunic, Janssen/Actelion, MAPI, Medimmune, Merck/EMD Serono, Novartis, Ono Pharmacia, Roche/Genentech, Sanofi-Genzyme, Teva Neuroscience, Wyeth (consulting fee). May H. Han: Novartis (consulting fee). Barry A. Singer: AbbVie, Biogen, Novartis, Sanofi Genzyme (consulting fee, contracted research). Acorda, Alexion, Celgene, EMD Serono, Genentech, Teva, TG Therapeutics (consulting fee). Alkermes, MedImmune, Roche (contracted research). Nina Jaitly, Scott Kolodny, Chelsea Elam, Xiangyi Meng: Novartis Pharmaceuticals Corporation (salary). Marina Ziehn: Novartis Pharma AG (salary). Bruce A C Cree: Akili, Alexion, Atara, Biogen, EMD Serono, Novartis, TG Therapeutics (consulting fee).*

Keywords: Disease-modifying treatments in MS

(DXT79)

Efficacy of Ocrelizumab Treatment on Cognitive Functions in Persons with Multiple Sclerosis

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Background: Ocrelizumab is the first treatment which could be use for progresive form of multiple sclerosis (MS). Generally ocrelizumab trials in MS investigate that side effect and safety properties. There are limited studies examine that effects of ocrelizumab on cognition in patient with MS (pwMS).

Objectives: The aim of this study was to evaluate the efficacy of ocrelizumab treatment on cognitive functions in pwMS.

Methods: In total, 35 pwMS included in this study. The participants clinical characteristics as MS type, disease duration and Expanded Disability Status Scale (EDSS) were recorded. Cognitive function was evaluated with The Brief International Cognitive Assessment for Multiple Sclerosis (BICAMS) battery, which consist of the Symbol Digit Modalities Test (SDMT), the California Verbal Learning Test-II (CVLT-II) and the Brief Visuospatial Memory Test-Revised (BVMT-R). The assessment was done at baseline and six month after the treatment.

Results: The avarage disease duration was 16.84±8.19 and EDSS score was 6.23±1.43. Participants clinical characteristics of the disease were 11.4% relapsing-remitting (RRMS), 57.1% (n=20) were secondary-progressive (SPMS), and 31.4% (n=11) were primary-progressive MS (PPMS). BVMT-R and CVLT-II scores were significantly increased at month 6 according to baseline assessment (20.71±7.85 vs 23.68±7.05, 45.03±11.97 vs 49.43±12.45, respectively) ($p< 0.05$). No significant differences observed between the baseline and month 6 in term of SDMT scores (34.37±14.95 vs 34.51±15.67) ($p>0.05$).

Conclusions: This study has suggested that ocrelizumab treatment could be affect positively on verbal and visual learning/memory. On the other hand, there was no positive or negative effect on information proccessing speed. In view of the fact that the majority of our patients are in progressive form, the protective or positive effect of ocrelizumab on cognitive functions is clinically important. Additionally, in order to better understand the effects of ocrelizumab treatment on cognitive functions, it is necessary to design studies with longer follow-up periods.

Disclosure: *Nothing to disclose.*

Keywords: Disease-modifying treatments in MS, Psychological issues and MS

Epidemiology and Genetics

(EPI01)

Determining the Effect of Early Versus Later Diagnosis of MS on Long Term Prognosis in the Real World Setting

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Background:

Early treatment of MS is recommended based on studies involving patients identified early with clinically isolated syndromes. Although early diagnosis and subsequent early treatment might be expected lead to a better outcome (lower EDSS), in a real world setting outcomes may be different concerning patients presenting (and treated) early after onset of symptoms (EP group) versus later (LP group). Other risk factors for worsening MS (poor recovery from first attack, motor onset etc) may be more predictive than EP vs LP status.

Objectives:

To compare characteristics of EP patients (with less than 1 year of symptoms at presentation) vs LP groups.

Methods:

Newly diagnosed MS patients seen up to 15 years divided as EP or LP were studied for attack type, frequency, and recovery and group statistics were applied.

Results:

There were 121 patients in the EP group, and 86 patients in the LP group. More patients with a high attack frequency in years 0-2 were seen in the EP group versus the LP group (45% vs 28%, p=0.014). The median time to treatment was shorter in the EP vs LP groups (by 32 months [8.91]), and we found no significant difference in disability long-term outcomes. Other clinical risk factors were evenly divided between EP and LP groups.

Conclusions:

These EP and LP groups were the same in terms of long term outcome. Earlier treatment and more active disease were seen in the EP group. We suggest a nuanced approach to interpretation of the “early diagnosis and treatment equals better outcome” rule.

Disclosure: *Jikku Zachariah, Rebecca Schorr, Tim Quezada: Nothing to disclose. Thomas F. Scott: Genentech, Biogen, Novartis, and Genzyme (consulting fee, contracted research, speakers bureau).*

Keywords: Disease-modifying treatments in MS, Epidemiology of MS, Natural history of MS

(EPI02)

Motor Impairment in Multiple Sclerosis: Analysis from the North American Registry for Care and Research in Multiple Sclerosis (NARCRMS)

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Background: NARCRMS is a longitudinal registry studying the course of MS in the disease-modifying era.

Objectives: To examine motor performance metrics of upper and lower extremity function in NARCRMS patients at enrollment.

Methods: Recruitment began in 2016 and by December 31, 2019, 662 patients were enrolled at 23 MS sites across the US and Canada. People with any sub type of MS within 15 years of disease onset and an EDSS of up to 6.5 are eligible for enrollment. Various clinical metrics are collected including motor performance for upper and lower extremities. Our initial observations about EDSS, 25-foot timed walk and the 9-hole peg test are reported below.

Results: EDSS and 25-foot walk times were available in 579 patients and upper extremity function in 571 patients. A mean walking speed of 4.9 seconds was recorded in patients with an EDSS of 0 (n=100). 5.0 seconds remained the mean speed until an EDSS of 3.0 (n=37) where a mean speed of 5.6 seconds was recorded. Walking truly became affected at an EDSS of 3.5 (n=25) where a mean speed of 6.1 seconds was recorded. Thereafter mean speed progressively declined at every EDSS increase. For an EDSS of 4.0 (n=25), mean speed was 7.9 seconds; for an EDSS of 4.5 (n=6), mean speed was 9.1 seconds and continued to increase until an EDSS of 6.5 (n=10) where mean speed was 16.8 seconds. For the 9-hole peg test, patients with an EDSS of 0 (n=96) had a mean speed of 19.4 seconds in the dominant and 20.7 seconds in the non-dominant hand. Hand function remained unimpaired until an EDSS of 2.0 and significant slowing occurred in patients with EDSS ranging from 2.5 to 6.5. For an EDSS of 2.5 (n=40), mean speed was 24.7 seconds in the dominant and 24 seconds in the non-dominant hand. For an EDSS of 4.0 (n=26), mean speed was 26.1 seconds in the dominant and 26.6 seconds in the non-dominant hand. For an EDSS of 6.5 (n=15), hand function had declined to a mean speed of 39.1 seconds for the dominant and 49.8 seconds for the non-dominant hand.

Conclusions: A linear correlation of the 25-foot walk speed to EDSS increases was remarkable, reiterating the commonly held belief that the EDSS is a "walking scale". Decline in hand function at an EDSS of 2.5 was unexpected since hands are often perceived to be unaffected early in MS and seldom observed as impaired by patients. Progressive decline of hand function at every EDSS increase would suggest that the 9-HP test is a good marker of declining hand function and should be included in clinical monitoring of patients.

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Keywords: Epidemiology of MS

(EPI03)

Increase in Family Recurrence on Patients Diagnosed with Multiple Sclerosis on the Years 2017-2019 in Hispanic Population of Puerto Rico

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Background: Multiple sclerosis (MS) is a neurodegenerative disease in which the immune system damages the central nervous system. The cause of MS is not known, but several studies look at environmental, immunologic, geographical and genetic factors. Thus, MS is not considered hereditary, but rather polygenic. However, there are several cases of patients with family history of MS in several relative degrees.

Objectives: Evaluate family recurrence of MS among patients diagnosed with MS on recent years in Puerto Rico (PR), including any type of degree relative.

Methods: For this, data from the Puerto Rican MS Registry (PRMS Registry) of all patients diagnosed on the years 2017, 2018 and 2019 registered at present in PR was analyzed.

Results: Overall 11.4% of patients had family recurrence of MS (45/396). For 2017, 9.7% (14/143) of patients had family history of MS of at least one family member. For 2018, 8.3% (14/167) of patients presented family history of MS. Lastly, for 2019 a total of 19.7% (17/86) of patients reported having family history of MS.

Conclusions: A slight increase in recurrence was observed when compared to previous study from 2013 to 2016 (10.2%). Further investigations need to be done to elucidate the genetic aspects of family recurrence of MS among the Puerto Rican population. The genetic mix of Caucasian, African and Taino races could have an influence on genetic risk among this

population. Also, it is important to keep this study ongoing to analyze familial risk in Hispanic population and compare it to other ethnic groups.

Disclosure: *Nothing to disclose.*

Keywords: Epidemiology of MS, Genetics and MS

(EPI04)

Diet Quality and Nutritional Adequacy of Micronutrients Among Relapsing-Remitting Multiple Sclerosis: An Analysis of Weighed Food Records

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Background: Multiple Sclerosis (MS) is a neurodegenerative disease that affects nearly 1 million in the U.S. Poor diet quality and micronutrient deficiencies have been reported in several studies and are associated with more severe disease. However, previous work has relied on diet screeners and questionnaires for data collection. Thus, these findings need to be repeated using more precise data collection instruments such as weighed food records.

Objectives: Weighed food records were used to evaluate diet quality and usual intake of micronutrients from people with diagnosed relapsing-remitting MS (RRMS).

Methods: As part of a dietary intervention study comparing the Wahls and Swank diets, three weighed food records were collected on two weekdays and one weekend day at a pre-randomization run-in visit from (n = 95) participants and again at a baseline visit from the (n = 87) non-excluded participants. Food records obtained from all participants were analyzed at the University of Minnesota Nutrition Coordinating Center. Diet quality was assessed using the Healthy Eating Index (HEI) which compares food groups and selected nutrient intakes to the Dietary Guidelines for Americans (DGAs). Mean intake of each micronutrient was calculated for each individual and adjusted using the National Cancer Institute (NCI) method to estimate usual intake. Usual intake of each micronutrient was then evaluated with the estimated average requirement (EAR)-cut point method for each life stage group and combined by weighted means to assess the overall nutritional adequacy of each micronutrient for the group.

Results: Preliminary analyses indicate that this cohort has a HEI score of 61 ± 12, which suggests that diet quality needs improvement. Furthermore, this cohort has high prevalence of inadequate intake for vitamins D 92.9%, E 61.4%, C 50.8%, A 35.3%, folate 31.0%, and B_6 22.8%, and minerals including calcium 49.8%, magnesium 45.8%, and zinc 19.5%. However, low prevalence of inadequate intake was observed for niacin 0.2%, thiamin 7.5%, riboflavin 3.0%, B_{12} 5.4%, phosphorus 2.0%, copper 6.6%, and selenium 1.0%.

Conclusions: Diet quality is low and intake of several micronutrients is inadequate in this RRMS cohort. These findings confirm observations from previous studies that poor diet quality and inadequate intake of micronutrients is common among those with RRMS. These findings may lead to new dietary strategies to manage symptoms and improve quality of life among those with MS.

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Keywords: Complementary/alternative therapies in MS, Comprehensive care and MS, Epidemiology of MS

Family and Caregivers

(FAM01)

Characterizing Predictors of Resilience Among Family Caregivers of People with Advanced Multiple Sclerosis Disability: Work in Progress

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Background: Providing ongoing support can adversely affect physical, psychological and social health of care partners of people with advanced multiple sclerosis (MS). However, some care partners have also reported positive experiences and benefits of MS caregiving (e.g., greater sense of commitment and pride in the role). This variability highlights the importance of understanding protective factors that can buffer against the adverse effects of caregiving. Psychological resilience describes positive adaptations to stressful situations and includes individual, community and societal level factors. Research in other caregiving contexts has shown that resilience is associated with improved health outcomes and lower levels of care partner burden. Unfortunately, there is limited research on resilience in the context of MS caregiving. Generating this knowledge is important to guide the development of interventions to enhance resilience and to identify individuals most likely to benefit from future intervention.

Objectives: To examine the relationships between resilience and a comprehensive set of individual, community and societal level factors in the context of MS caregiving.

Methods: A cross-sectional survey study. We are collecting data as part of a pilot randomized controlled trial evaluating the feasibility and efficacy of a dyadic physical activity program for people with advanced MS and their care partners. Eligibility criteria include care partners who: 1) are ³18 years old; 2) provide ³1hr/day of care; 3) are inactive; 4) are asymptomatic; and 5) are able to communicate in English. Care partners will complete demographics and general health questionnaires. The following scales will also be administered: 1) Caregiving Tasks in MS Scale; 2) Connor-Davison Resilience Scale; 3) Interpersonal Support Evaluation List-12; 4) Coping with MS Caregiving Inventory; 5) Measure of Experiential Aspects of Participation; and 6) Godin Leisure-Time Exercise Questionnaire. We will conduct regression modelling to identify predictors of resilience among care partners.

Results: Data collection is ongoing. Anticipated completion date is March 2020. We will present findings on resilience and associated factors among MS care partners.

Conclusions: Resilience may be an important protective factor against the adverse effects of MS caregiving. We anticipate that the findings from this study may have implications for interventions designed to enhance and sustain resilience among MS care partners.

Disclosure: *Nothing to disclose.*

Keywords: MS and the caregiver/family

(FAM02)

Understanding Units of Energy: Key to Communicating Multiple Sclerosis Fatigue

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Background:

Fatigue, defined as the difficulty or inability to perform tasks due to a lack of sufficient energy, is one of the key symptoms of Multiple Sclerosis (MS). The level of fatigue is difficult to quantify and explain to a person without the condition. Interactions between persons with MS (PsWMS) and those without (PsWO) with whom they have interpersonal relationships can be damaged by this lack of understanding.

The Roy Adaptation Model (RAM) (Roy & Andrews, 1999) provides a nursing framework through which to assess, intervene and evaluate the effective communication between PsWMS and PSWO. The RAM views persons as adaptive entities in constant interaction with their environment. One portion of the theory, the interdependence adaptive mode, focuses on the communication between a person and his or her significant other/support group. Clear

understanding of the message sent and received and the ensuing healthy adaptations to their interactive communication resulting in behavioral change are the goals.

Objectives: By quantifying the amount of energy each activity takes, PsWMS will be able to communicate more clearly their level of energy and, inversely, their level of fatigue. Relational stress will decrease and communication between PsWMS and PsWO will improve.

Methods: A MS support group comprised of 23 persons, some with MS and some without, participated in a two-hour educational, interactive session, which focused on defining units of energy and describing how many may be needed for both activities of daily living and special events. The PsWO "tried on" different symptoms of MS throughout the session to gain a better understanding of the challenges facing the PsWMS. At the same time, the PsWMS focused on self-assessment and became more aware of the frustrations expressed by the PsWO. Both subgroups practiced active listening techniques.

Results: After two months, all 23 persons reported improved relationships due to decreased stress and a better understanding of the effects of MS.

Conclusions: Teaching a simple method of communicating MS fatigue greatly improved the quality of life of PsWMS and those with whom they interact. Using units of energy within conversations improved communication and enabled more positive interdependent interactions with caregivers, family members and their colleagues in the workplace.

Roy, Sr. C. & Andrews, H.A. (1999). The Roy Adaptation Model (2nd Ed.). Stamford, CT: Appleton and Lange.

Disclosure: *Nothing to disclose.*

Keywords: Fatigue, Management of activities of daily living in MS, MS and the caregiver/family

Internet and Information Services

(IIS01)

North American Registry for Care and Research in Multiple Sclerosis (NARCRMS) Model for Implementing Openclinica Insight for Data Sharing and Visualization

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Background: NARCRMS is a clinic-based longitudinal registry of sites located in the United States and Canada. Active since 2015, the registry is a public-private partnership aiming to improve MS care and understanding as a database of clinical records and patient-centered outcomes. With enrollment, yearly follow-up and exacerbation-based visits, patients provide demographic, medical history, attack history, and health productivity information supplemented with physician-collected physical and cognitive assessments. In just a few years the registry has generated several hundred thousand points of data on a wide variety of health-related topics from the current 22 participating sites. The registry includes data from standardized interviews, physician evaluations, and is adding self-administered patient reported outcomes in the coming months.

Objectives: To develop a model to share aggregated data from individual sites to enable participating sites and industry partners the ability to view and analyze larger, multi-site datasets for research and exploration.

Methods: OpenClinica is an open-source and software-as-a-service (SaaS) electronic data collection (EDC) system most often used for data collection and data management in a clinical setting. OpenClinica Insight, built on the open-source Metabase platform, is a data reporting and sharing tool available as part of OpenClinica's Enterprise system that connects directly to the EDC database and allows real-time data access, visualization, and downloading. To implement Insight, the team coordinated with project leadership, industry, and cooperating investigators to develop a process for defining roles and relationships, defining appropriate summary charts and graphs to summarize collected data, and defining data access parameters and restrictions.

Results: OpenClinica Insight provides a platform to leverage limited standardized patient-derived data on a prospective basis. The platform is useful and end-user friendly and allows for efficient information sharing across the pool of geographically-diverse clinical research sites to provide insights into local, regional, and continental patterns and standards of MS care.

Conclusions: OpenClinica Insight is a powerful tool to report information from OpenClinica Enterprise and the model developed from NARCRMS should serve as an example for integrating informatics from large databases developed to study natural history of various chronic disorders such as multiple sclerosis.

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Keywords: Epidemiology of MS

Imaging

(IMG01)

Conformance to CMSC MRI Guidelines in a Real-World Multi-Center MRI Dataset

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Background: Acquiring magnetic resonance images (MRI) in a standardized way allows early and accurate diagnosis of multiple sclerosis (MS) and patient follow-up. The CMSC guidelines for MR imaging suggest a standardized protocol to improve the diagnosis and routine follow-up of MS.

Objectives: This study evaluates how many MRI acquisitions from a real-world dataset of MS patients satisfy the CMSC brain MRI guidelines (2018 revision). In particular, for every individual MR sequence, it is assessed how well the guidelines are met.

Methods: CMSC brain MRI guidelines of 2018 impose that 4 different scans should be acquired: a 2D or 3D (sagittal and axial) fluid-attenuated inversion recovery (FLAIR); a 2D axial or 3D T2 weighted scan, an axial 2D diffusion-weighted image (DWI) and a 3D inversion-recovery prepared (IR-prep) gradient-echo T1. For every scan, an in slice pixel resolution ≤ 1mm x 1mm, slice thickness ≤ 3mm with no slice gap, as well as whole-brain coverage are required.

These requirements are checked on a multi-center MRI dataset from the US, consisting of 1233 sessions, acquired in 581 different centers/scanners from 2018 onwards.

Results: None of all 1233 MRI sessions fully complied with the guidelines.

For the T1 sequence, only 8% satisfied the criteria. For the other data, 23% did not have a T1 sequence, 73% had a too large slice thickness, 71% had a too large pixel size, 56% had a slice gap, 48% did not use an IR-prep gradient echo.

For FLAIR, only 18% satisfied the requirements. For the other data, 8% and 21% missed the axial and sagittal FLAIR acquisition respectively and 82% had too large slice thickness, slice gap or too large pixel size.

For the T2 sequence, only 7% satisfied the criteria. The most important reason for failing was a too large pixel size (92% of unsatisfying images).

17% of the scans had no DWI, 1% of all scans had a good DWI, the other 81% had a too large pixel size.

If a post-gad T1 was provided, 29% satisfied the guidelines. Of all post-gad T1 sequences that did not comply, 70% had a too large pixel size, mostly in combination with suboptimal slice thickness and/or slice gap.

Conclusions: In a real-world MRI dataset of MS patients, the conformance to the CMSC brain MRI guidelines was extremely low. The main reason was the use of a too large pixel size, mostly in combination with a too large slice thickness and a slice gap, which could be due to speeding up the protocol.

Disclosure: *Sophie Vercruyssen, Arne Brys, Melissa Verheijen, Brandon Steach, Eline Van Vlierberghe, Diana M. Sima, Dirk Smeets: icometrix (salary).*

Keywords: Imaging and MS

(IMG02)

Optic Nerve Head Volume Is Significantly Decreased in Pediatric MS and Not Pediatric Mog-Related Disorders

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Background: Youth with MS or myelin oligodendrocyte glycoprotein (MOG)-associated disorders exhibit changes in Retinal Nerve Fiber Layer (RNFL) and Ganglion Cell Inner Plexiform Layer (GCIPL) thickness, but knowledge about abnormalities in optic nerve head (ONH) morphology in these groups is lacking.

Objectives: To compare ONH characteristics of youth with MS or MOG-associated disorders with a healthy control (HC) population.

Methods: Standardized OCT data (Cirrus HD-OCT (Carl Zeiss Meditec, Dublin, CA)) were collected on HC (n=27(16F), median age 15y (IQR1.3)), youth with MS (n=17(11F), 16.9y (1.5), disease duration 2.6y (2.8)), and youth with MOG-related disorders (n=13(11F), 11.5y (4.2), 1.7y(1.3)). ONH parameters (total ONH volume (TV), Bruch's membrane opening (BMO) region volume (BMO-Vol), and BMO minimal rim width (BMO-MRW)) were computed by

triangulated 3D surface reconstruction. Mean peripapillary RNFL and macular GCIPL were derived from manufacturer's fully-automated segmentation software, and results manually reviewed where necessary. Multivariable mixed effects models were used to model the five ONH parameters between groups, accounting for age at OCT, eye-specific number of optic neuritis episodes, and a subject-specific random intercept. Results were Bonferroni adjusted for multiple comparisons (p = 0.01).

Results: MS participants showed lower ONH TV (-.24 mm3,SE.073,p=.002), BMO-Vol (-.22 mm3,SE.083, p=.012), and BMO-MRW (-.42 dMRW,SE.014,p=.004) compared to HC. ONH parameters were not different in MOG patients versus HC. Neither RNFL nor GCIPL were significantly different between HC and MS. GCIPL was lower in MOG than HC (-7.9 µm,SE3.05,p=.012).

Conclusions: Our analysis showed ONH volume loss in pediatric MS despite no significant differences in RNFL or GCIPL in comparison to HC. These differences, except for a lower GCIPL, were not present in MOG versus HC. ONH analysis may therefore be superior to RNFL or GCIPL in detecting anterior visual pathway injury in MS early in the disease course. Larger studies are needed to confirm these findings.

Disclosure: *Giulia Longoni, Tara Berenbaum, Michael J. Wan, Arun Reginald, Donald Mabbott, E Ann Yeh: Nothing to disclose. Sunil K. Yadav, Ella M. Kadas: Nocturne GmbH (co-founder and shareholder). Alexander Brandt: Nocturne GmbH and Motognosis GmbH (co-founder and shareholder).*

Keywords: Imaging and MS

(IMG03)

Cerebellar Connectivity Is Associated with Verbal Memory Impairment in Multiple Sclerosis

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Background: Network connectivity is disrupted in multiple sclerosis (MS) and is related to cognitive function. Verbal memory impairment is common in MS yet the underlying neuropathology is still unknown. Recent research suggests cerebellar involvement in verbal memory and the cerebellum is adversely affected by MS. Thus, investigating the role cerebellar dysfunction plays in MS-related abnormal connectivity and verbal memory impairment may aid in understanding MS-related verbal memory impairment.

Objectives: Investigate the relationship between cerebellar-cortical connectivity and verbal memory impairment in MS.

Methods: 45 MS and 23 healthy controls (HC) completed a verbal memory task (Selective Reminding Task, SRT) and underwent magnetic resonance imaging. Resting-state (RS) functional connectivity analysis and diffusion kurtosis imaging were used to assess functional and structural connectivity, respectively.

Results: The MS group performed significantly worse on SRT Trial 1 (t[66]=2.18, p=.033), SRT Trial 3 (t[66]=2.20, p=.031), SRT Trial 6 (t[66]=2.44, p=.017), and SRT Delayed Recall (t[66]=2.27, p=.026). Resting -state analysis of cerebellar-cortical connectivity revealed significant differences between the cerebellum and several cortical areas. In MS, higher connectivity was observed between the cerebellum and superior frontal gyrus, precuneus, supramarginal gyrus, medial frontal gyrus, inferior parietal lobe, cingulate, and parahippocampal gyri (p=.05, FWE-corrected). Correlation analysis within the MS group revealed significant correlations between SRT Delayed Recall scores and connectivity values between the cerebellum and parahippocampal gyrus, fusiform gyrus, insula, cingulate, inferior frontal gyrus, uncus, middle temporal gyrus, and angular gyrus (p=.05, FWE-corrected). We observed higher connectivity in memory-impaired MS patients between the cerebellum and the left parahippocampal gyrus compared to memory-preserved MS patients. Diffusion analysis showed that axonal volume of the middle cerebellar peduncle significantly explained variability in SRT Delayed Recall scores in MS patients over and above age and education (F[1,32]=4.62, p=.039, R^2=.17, ΔR^2=.12).

Conclusions: Abnormal resting-state and structural connectivity between the cerebellum and cortical areas, specifically the left parahippocampal gyrus, may contribute to verbal memory impairment observed in MS.

Disclosure: *Mark D. Zuppichini, Kathryn West, Dinesh Sivakolundu, Bart Rypma: Nothing to disclose. Darin T. Okuda: Acorda (speaker fees). Biogen (contracted research). EMD Serono, Genentech, Novartis, TEVA Neuroscience (consulting fee). Genzyme (consulting fee, speaker fees).*

Keywords: Imaging and MS, Memory, Psychological issues and MS

(IMG04)

The Association between MRI Brain Volumes and Computerized Cognitive Scores of People with Multiple Sclerosis

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Background: Cognitive impairment is common and disabling among people with multiple sclerosis (PwMS), but is not often monitored or only partially screened due to complexity of evaluation. Computerized cognitive assessment facilitates the incorporation of multi-domain cognitive monitoring into routine clinical follow up.

Objectives: To explore the associations between brain volumes and cognitive scores of a computerized cognitive assessment battery (CAB, NeuroTrax) among people with multiple sclerosis.

Methods: Participants were tested with the CAB and underwent brain MRI within specified time intervals. The global cognitive score (GCS) is the average of age and education adjusted scores of the various cognitive domains (memory, information processing speed, attention, executive function, motor and verbal). Whole brain volume (WBV), Gray matter volume (GMV), White matter volume (WMV), Thalamic volume, Hippocampal volume, white matter lesion volume and lateral ventricles volume were assessed by IcoMetrix, a fully automated tissue and lesion segmentation and quantification software, that uses 3D T1-weighted and fluid-attenuated inversion recovery (FLAIR) MRIs.

Results: 201 PwMS were tested with both CAB and MRI within 180 days (Age: 52.3±11.1, 143 (71%) female). Significant correlations were found between the GCS and WBV, WMV, GMV, Thalamic volume and FLAIR lesion volume (Spearmans rho's: 0.33, 0.3, 0.43, 0.4, -0.26, $P<0.01$, respectively). Correlation coefficients remained significant but decreased as the time between MRI and CAB increased. The number of impaired cognitive domains was also associated with both lesion volume and GMV (rho=0.25, -0.44; $P<0.05$, <0.01, respectively) .The only cognitive domain score that was associated with Hippocampal volume was memory (rho=0.27, $P<0.05$).

Conclusions: Computerized cognitive scores are significantly associated with quantified MRI. These findings demonstrate the added information that can be derived from integrating digital assessment tools into the routine clinical assessment of PwMS.

Disclosure: *Daniel Golan, Jared Srinivasan, Olivia Kaczmarek, Jonathan Bautista, Marijean Buhse, Lori Fafard, Timothy Fratto: Nothing to disclose. Myassar Zarif: Acorda, Biogen, Genzyme, Teva (speakers bureau). Barbara Bumstead: Biogen, Genzyme (speakers bureau). Jeffrey Wilken: Biogen (contracted research). EMD Serono (speakers bureau). Genzyme (contracted research, speakers bureau). Cynthia Sullivan: Roche (contracted research). Eline Van Vlierberghe, Diana Sima, Wim Van Hecke: icometrix (salary). Mark Gudesblatt: Acorda, Amgen, Medtronic, Saol Therapeutics (speakers bureau). Biogen, EMD Serono, Novartis, Sanofi, Teva (contracted research).*

Keywords: Equipment in MS, Imaging and MS, Natural history of MS

(IMG05)

Analysis of Demyelinizing Injuries in Magnetic Resonance in People with Multiple Sclerosis

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Background: Multiple Sclerosis (MS) is a demyelinating autoimmune disease in which the immune system affects the myelin sheath of neurons, resulting in several clinical manifestations. Magnetic resonance imaging (MRI) is essential for understanding MS, as it allows objective visualization of both acute and chronic lesions. Signs and symptoms of MS depend on the location of the lesions and often impact on people's quality of life.

Objectives: To analyze MRI lesions in a group of individuals with MS.

Methods: Ten individuals with MS participated. Retrospective MRI analyzes were performed in the database over a period of 1 year with the Doctor Neurologist of the Civil Social Institution for MS, in the city of São Paulo, in 2019, where the individuals present MRI at the consultation.

Results: Data from both sexes were used, being 60% women and 40% men, minimum age of 29 and maximum of 59. Of these individuals, 50% had the recurrent remitting clinical subtype, 30% secondarily progressive and 20% primarily progressive, and 40% had been diagnosed for over 10 years. Regarding EDSS, the majority (70%) were between 4.5 and 6.5 and 50% had outbreaks for more than three years. The images revealed white matter lesions, T2 and FLAIR hyperintensities, with contrast uptake in T1-weighted images, with predominantly juxtacortical involvement with 12%, 11% in the corpus callosum, followed by 8% in the temporal, peri-ventricular regions. 6% in the cervical and thoracic regions, 4% in the subcortical, frontal, cerebellar, parietal regions, and finally 2% in the bridge, bulb, and thalamic regions.

The most frequent types of injuries are: atrophy 12% and Black roller 4% With less incidence in the bridge and bulb.

Conclusions:

This paper suggests some areas that are most affected by the disease through MRI, and in our study population, the greatest involvement was brain and a small percentage was at the medullary level, generating motor, sensory and cognitive impairment.

Studies of this kind favor health professionals in understanding the evolution of the disease and the development of neurorehabilitation techniques.

Further studies in this line should be conducted with a larger number of participants, so that we can have a better idea about the incidence of the affected areas.

Disclosure: *Nothing to disclose.*

Keywords: injuries, Imaging and MS

Multidisciplinary Care

(MDC01)

Social Assistance Intervention in Multiple Sclerosis

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Background: People with Multiple Sclerosis (PwMS) have a complex symptoms and different types of needs. These demands include how to manage the burden of physical disability as well as how to organize daily life, restructure social roles in the family and at work.

Objectives: To identify difficulties and obstacles experienced by PwMS, highlighting the work of Social Service in promoting physical, psychological and social well-being.

Methods: The sample involved 113 PwMS, 82 women and 29 men, aged 17 to 77 years (mean=41/SD=11.38). All answered the semistructured Sociodemographic Questionnaire containing 30 questions, developed specifically for this population.

Results: Despite the highlighted needs, lack of knowledge about treatment, rehabilitation and maintenance of quality of life was widely identified among the participants. In this sense, specific referrals and specializes guidance pertinent to our country were carried out as follows: n=117/100% health (high cost medicines), n=35/30% social security (retirement), n=23/20% education (educational institutions), n=59/50% judicialization (medicines demand in lawsuits).

Conclusions: The individual reception procedure was necessary and sensitive for understanding the demands through the questionnaire. The difficulties identified in this study determined social assistance actions directed to the development of joint actions with multi and interdisciplinary teams, which directly impacted the quality of life of patients with all types of MS.

Disclosure: *Nothing to disclose.*

Keywords: Management of activities of daily living in MS, MS and the caregiver/family

(MDC02)

Is a Two Week Intensive Day Program an Effective Approach to Provide Outpatient Services for People with MS?

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Background: A unique two-week intensive MS day program rehabilitation model was initiated in 2012 and continues to evolve. The goal of the program is to educate and provide patients, families and caregivers with a structured plan to improve overall health and wellness. Our interdisciplinary team would like to share "lessons learned the hard way" over the past 7 years and to report the most recent patient outcomes.

Objectives:

1. Identify key factors which may indicate appropriateness for patient enrollment in an intensive day program.
2. Identify "lessons learned" over the past seven years.
3. Present results of objective patient outcome measures.

Methods: Patients are evaluated to determine appropriateness for participation in a two-week intensive day program (DP). To qualify for DP, they must require skilled services for Physical Therapy (PT), Occupational Therapy (OT), Speech Therapy (ST) and Wellness. Additionally, they may also receive Nursing, Counseling and Vocational Rehabilitation as appropriate. It is mandatory that a caregiver/family member be present for all sessions. Pre and post outcome measures used to assess change include Modified Fatigue Impact Scale (MFIS), Fatigue Severity Scale (FSS), Symbol Digit Modalities Test (SDMT), Nine-hole peg test (9HP) and Timed 25 ft walk (T25ft).

Results: EDSS ranged from 2.5 to 9.0 with 67% of patients having EDSS 5.0 or greater. Patient and family feedback regarding DP has generally been positive. The most frequent negative comments are that too much information is presented and becomes overwhelming, not enough rest breaks are given and the days are too long. Despite reports of being too intensive, a large majority of participants have shown progress on outcome measures. Percentage of patients whose scores improved are as follows; MFIS 70%, FSS 90%, SDMT 70%, 9HP 67% (right) 87% (left) and T25ft 75% (note 3 patients went from being non-ambulatory to walking with a rollator). A more detailed report of the data will be ready at the time of presentation.

Conclusions: Multiple factors need to be considered prior to recommending DP to persons with MS. To achieve success, patients/families must be willing to modify old behaviors and staff must adapt session intensity so as not to overwhelm or over fatigue patients. An interdisciplinary community outing at the end of the first week has proven valuable to patients/families. Changes to the structure of day program have been incorporated based on patient feedback. Re-evaluations two months post DP are encouraged.

Disclosure: *Nothing to disclose.*

Keywords: Comprehensive care and MS, Day Program Outcomes

(MDC03)

The Waiting Room: A Successful Experience in the Multiple Sclerosis Care and Treatment Center (CATEM)

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Background:

The constant waiting of patients for the call for medical consultation is a reality in the Brazilian public service. The National Policy for Humanization (NPH) of the Brazilian Ministry of Health (MH) advocates providing welcoming, strengthening and wholesome care, with the adoption of measures and communication among multi-professional teams. One of the practices utilized by the health team to share experiences, feelings and knowledge between patients of professionals is the Waiting Room Group. The Multiple Sclerosis Care and Treatment Center (MSCTC), established in 1997 at the Neurology Clinic of Santa Casa de Sao Paulo, attends through the Unified Health System (UHS) every Friday morning and has about 500 registered patients who make use of several therapies for treatment of Multiple Sclerosis – MS. To minimize the waiting period, the "Waiting Room" project was created in 2013, consisting of patients, family members, caregivers, social worker, nurse, physiotherapist, psychologist, and neuropsychologist, among others, in order to provide a welcoming space to minimize anxiety and fear, advise on their rights, inform about the disease and its complications, types of treatment, importance of adoption and adherence of exercise routines, and hospital policy and routines, providing patients, family members and caregivers with a space of power and affection in order to have a more active and participative role in their treatment.

Objectives: To describe the experience of the Waiting Room Group as part of humanized care for MS patients, their family members and caregivers

Methods: Welcoming, integration and interaction are the key words: the earlier patients talk about and share their experiences with those that are starting their treatment, minimizing their anxiety and doubts. The doctor, psychologist, social worker, nurse and physiotherapist, participate in all meetings, as well as other invited professionals. During the meetings, the doubts presented by the participants are clarified and provide topics for discussion in the next meetings.

Results: not applicable

Conclusions: This project has been developed for six years and has been successful, with an average participation of 500 patients / year.

Disclosure: *Nothing to disclose.*

Keywords: Comprehensive care and MS, Interdisciplinary Team, MS and the caregiver/family

(MDC04)

MS Brain Health Global Quality Standards: MS Nurses' Role in Development and Implementation

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Background:

'Time matters at every stage of multiple sclerosis (MS)' is the key message of the evidence-based initiative MS Brain Health.[1]

Objectives:

We aimed to define standards for timely diagnosis and treatment, based on the widely endorsed MS Brain Health recommendations,[1] for use in MS clinics worldwide.

Methods:

An international panel of MS neurologists participated in an iterative modified Delphi process to define 'core', 'achievable' and 'aspirational' time frames for key steps in the MS care pathway. A multidisciplinary reviewing group (RG), including MS nurses, provided early insights and feedback on whether the final standards were appropriate. The consensus standards were incorporated into an Excel-based quality improvement (QI) tool for potential use in MS clinics worldwide: a prototype of this tool has been piloted in three MS clinics.

Results:

The final consensus standards covered 6 aspects of the care pathway: symptom onset, referral and diagnosis, treatment decisions, lifestyle, disease monitoring and managing new symptoms.[2]

Nine MS nurses from 8 countries participated in the RG. For 56/76 (73.7%) of the standards, the majority considered the targets to be 'about right'. Overall, no 'core' standards were considered too ambitious and no 'aspirational' standards were considered not ambitious enough by participating MS nurses.

In one case study, to be presented, the local MS nurse led a QI program for the MS service, based on the standards. This included engaging and securing support from the multidisciplinary team, entering data on service delivery, reviewing results and developing strategies for care improvement based on the findings. As a result of this pilot, the MS service made changes to local processes for care delivery and record-keeping.

Conclusions:

MS nurses play a pivotal role in service improvement. The nurses in the RG agreed with the consensus standards for brain health, and the subsequent nurse-led pilot of the QI tool was based on the findings. This provides a promising foundation for wider dissemination of the quality standards, with MS nurses as a focal point for facilitating their use locally. Widespread roll-out of the MS Brain Health QI tool will enable MS clinics to collect data for local insights and, as part of the wider MS community, to participate in national and international benchmarking.

References:

1. Giovannoni G *et al. Mult Scler Relat Disord* 2016;9 Suppl 1:S5–S48
2. Hobart J *et al. Mult Scler* 2019;25:1809–18

Disclosure: *Amy Bowen, Kathleen Costello: Nothing to disclose. Jodi Haartsen: Biogen, Merck, Roche (consulting fee). Lucy Eberhard: Oxford PharmaGenesis Ltd (employee of oxford pharmagenesis ltd). George Pepper: Biogen, Novartis, Oxford PharmaGenesis Ltd, Teva (consulting fee). Jeremy Hobart: Acorda, Asubio, Bayer Schering, Biogen Idec, F. Hoffmann-La Roche, Genzyme, Merck Serono, Novartis, Oxford PharmaGenesis Ltd, Teva (consulting fee, honoraria, support to attend meetings or research support). Gavin Giovannoni: AbbVie, Atara Bio, Canbex Therapeutics, Five Prime Therapeutics, GlaxoSmithKline, GW Pharma, Oxford PharmaGenesis, Protein Discovery Laboratories, Roche, Synthon, Teva Neuroscience, UCB (consulting fee). Bayer HealthCare, Biogen, Merck, Merck Serono, Novartis, Sanofi Genzyme (consulting fee, grant/research support).*

Keywords: Comprehensive care and MS, MS quality standards, Nursing management in MS

(MDC05)

Implementation of a Pharmacist-Led Immunization Program in a Center for Comprehensive Multiple Sclerosis(MS) Care

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Background: In 2019, the American Academy of Neurology issued a practice guideline update for vaccinations in patients with Multiple Sclerosis. In this guideline, they recommend providers "assess and reassess vaccination status of patients with MS before prescribing immunosuppressive or immunomodulating (ISIM) therapy and should vaccine these patients." Also in 2019, eculizumab was the first FDA treatment approved for Neuromyelitis Optica Spectrum Disorder (NMOSD). Prior to starting, the FDA requires patients receive 2 types of meningococcal vaccines (MenACWY plus MenB-4C or MenB-FHbp) at least 2 weeks prior to starting eculizumab. MS centers need to create an efficient process to ensure patients receive vaccines in a timely fashion to reduce harm from vaccine preventable diseases and not delay start of patient's disease modifying therapy (DMT).

In 2002, Pennsylvania allowed pharmacists to provide immunizations to patients under a collaborative practice agreement or a direct order from a provider. At the Hospital of the University of Pennsylvania, there are 2 clinical pharmacists dedicated full-time to the MS Center. Little information in the literature addresses providing immunizations to MS and NMOSD patients prior to starting DMTs and the utilization of MS clinical pharmacists and a health-system based specialty pharmacy in providing this unmet need.

Objectives: The purpose of this quantitative pilot study will be to review the results of a pharmacist-led immunization program imbedded within a 16 provider MS clinics

Methods: Patients will be identified by provider referrals and pharmacist comprehensive chart reviews of newly diagnosed patients and patients starting ISIM and eculizumab therapy.

Results: Data will be analyzed with descriptive statistics.

Conclusions: It is anticipated this pilot study will increase rates of vaccination of MS patients, reduce time to start DMT, and increase awareness of vaccine preventable diseases.

Disclosure: *Lauren Long: Celgene, Novartis (consulting fee). Ryan Fuller: Nothing to disclose.*

Keywords: Comprehensive care and MS, Disease-modifying treatments in MS, Preventative Health

(MDC06)

The African American Experience and Multiple Sclerosis

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Background: Incidence rates of MS have been found to be higher in both Black males and Black females versus White males and White females. In particular, Black females have a 47% higher risk for MS when compared to White females. Disease progression is significantly faster

in Black MS patients in both brain and retinal measures. MRI scans show whole brain and gray and white matter atrophy to occur twice as fast in African Americans compared to Caucasian Americans. African American patients also show quicker atrophy of the thalamus, possible link to cognitive impairment. Furthermore, African Americans are dying from MS at an earlier age, suggesting that MS burden weighs disproportionately across race demographics. To fully understand, the MSAA launched the African American MS Advisory Board.

Objectives: The African American Experience & Multiple Sclerosis initiative included 11 MS clinicians and 16 African Americans impacted by MS. The meeting's objectives were to: 1) Create a dialogue allowing both groups to share their views on the problems that African Americans living with MS are facing; 2) Evaluate programmatic initiatives that addresses the unmet needs; 3) Gather from the meeting to aid in the development of an actionable plan, tailored educational offerings, and services provided; and 4) Identify next steps to continue building on the work of the African American committees.

Methods: Participants attended a half-day meeting, sharing their views on problems African Americans living with MS are facing. Sessions included moderated discussions and a brief presentation, emphasizing on the need for research and the importance in developing programmatic initiatives.

Results: Key findings from the meeting in Atlanta, elucidated the aforementioned performance gaps experienced by MS clinicians responsible for treating African Americans living with MS. Characteristics of MS patients less likely to see neurologists include the following: 1) Lack of health insurance, 2) Lower income, 3) African American, 4) Living in rural areas, and 5) Illness longer than 15 years. Conversely, patients cared for by a neurologist are more likely to: 1) Undergo diagnostic tests, 2) Undergo treatment-related tests, 3) Be treated with disease modifying therapies, 4) Receive medication for symptoms, and 5) Report their providers had a treatment plan. The presence of these gaps requires behavioral change on the behalf of MS clinicians that will appropriately address barriers resulting in initial treatment delays, and a much faster disease progression in Black MS patients.

Conclusions: Data from this comprehensive initiative will drive the materials and information for a set of multifaceted interventions to improve the knowledge, competence, and/or performance of MS clinicians that are currently, or, have the potential to treat Black MS patients. The anticipated result is to better identify and detect early signs of disease progression and timely therapeutic intervention.

Disclosure: *Nothing to disclose.*

Keywords: African American and MS, Comprehensive care and MS

(MDC07)

The Impact of the Nurse Practitioner Model of Care within Multiple Sclerosis

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Background:

The Nurse Practitioner (NP) within Australia and within Multiple sclerosis (MS) is designed to improve outcomes for people with MS through the adoption of strategies that optimize therapeutic decision-making and improve communication around benefit and risk. The NP model is a safe and effective use of resources that enhances patient related outcomes.

Objectives:

There is much evidence in the literature to support the NP internationally however within Australia the model has been limited with numerous barriers to fulfil the role to its full potential. The objective of this data set is to compare and contrast the effectiveness and safety of the NP role in the MS setting.

Methods:

A cohort analysis of patients with a primary diagnosis of Multiple Sclerosis was conducted over a period of 12 months. This analysis assessed a diverse range of end points; including time to treatment, shared decision-making practices, benefit and risk discussion and access to care.

A comparison was made between the NP and specialist neurologists in a large neurology department of a quaternary hospital within Brisbane, Queensland, Australia. A simple random sampling process was utilized to generate 168 patients from each group. Further statistical analysis will be completed upon this data set.

Results:

Of 168 patients, a greater proportion were seen within 30 days of referral to a NP (59%) contrasted with a neurologist (11%). It was found that of patients who saw a NP versus a neurologist, there was increased discussion of potential benefit and risk (40% and 11%), increased initiation of disease modifying therapy (50% compared with 21%), more frequent identification of relapses (23% versus 4%) and a greater appointment attendance in the NP cohort (99% and 82%). When examining the access to treatment between the two cohorts, it was found that 75% of the NP cohort received treatment within 0-60 days, as opposed to 65% of the neurologist cohort. Both cohorts were comparable in terms of hospital readmissions and emergency department presentations within 90 days of clinician consultation.

Conclusions:

The results highlight the benefit of the NP role within a neurology practice in an Australian setting; it was evident that the NP provided timely access to care and treatment. NPs remain a safe, effective and valuable role within the MS community. Further resources as well as research should be implemented to support and evaluate this role within hospitals and communities across Australia.

Disclosure: *Nothing to disclose.*

Keywords: Comprehensive care and MS, Disease-modifying treatments in MS, Nursing management in MS

(MDC08)

Late-Onset Multiple Sclerosis: Comorbidity and Disease Progression

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Background: Late-onset multiple sclerosis (LOMS) defined as multiple sclerosis (MS) with clinical onset after the age of 50. Previous studies have demonstrated that late onset is a poor prognostic factor for MS. Moreover, several comorbidities such as hypertension, diabetes and dyslipidemia were reported in association with poor clinical outcome in MS patients. Although the prevalence of comorbidity is increased in the aging population, the roles of comorbidity in LOMS has not been explored.

Objectives: To evaluate the influence of comorbidities in LOMS

Methods: This retrospective study included 38 MS patients with clinical onset after the age of 50. Demographic, clinical, radiologic, and laboratory findings were collected. The survival analysis was performed to identify the comorbidities which associated with losing of the no evident disease activity (NEDA) status. Relapse, Expanded Disability Status Scale worsening, or new T2 or T1 gadolinium-enhancing lesions on MRI resulted in loss of NEDA status.

Results: The median follow up was 26 months (IQR 12-45.75 months). Forty-five percent of participants remained on NEDA status until the last follow-up. Hypertension (HTN) is significantly increased the risk of disease progression (HR 4.36, 95%CI 1.39-13.66, p 0.012). Moreover, the risk of losing NEDA in poor-controlled HTN patients is higher than in patients with well-controlled HTN (HR 7.67, 95%CI 1.01-58.12, p 0.049). Interestingly, there was no significant difference in disease progression risk between well-controlled HTN and normotensive LOMS patients (HR 1.58, 95%CI 0.28-9.01, p 0.608). Diabetes, dyslipidemia, coronary artery

disease, stroke, obesity, hypothyroidism, depression and anxiety were not significantly associated with MS progression in the late-onset population.

Conclusions: Our cohort study suggests that HTN is a modifiable risk factor of disease progression in LOMS. Previous studies have demonstrated that HTN can potentiate neurodegenerative process. Larger prospective studies are needed to further explore the interaction between HTN and disease-modifying therapy and the effect of antihypertensive agents.

Disclosure: *Smathorn Thakolwiboon, Pavida Pachariyanon, Jie Pan, Amputch Karukote, Gyeongmo Sohn: Nothing to disclose. Mirla Avila: Biogen, Genentech, Genzyme (education). Celgene (educaiton).*

Keywords: Comorbidity, Comprehensive care and MS

(MDC09)

Comparing Patient Perceptions on Multiple Sclerosis Management and Care: A Sub-Analysis of Geographic Differences

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Background: The MS in the 21st Century initiative is led by a Steering Group of international multiple sclerosis (MS) specialists and patient advocates with a current focus of improving education and communication between healthcare professionals and people with MS (PwMS).

Objectives: To compare the perceptions of PwMS on MS management and care across two geographical regions: Europe, and North America (US and Canada). Particular emphasis was on patient support at diagnosis, treatment decisions, and communication.

Methods: An electronic survey was developed to gain insight into patients' opinions on unmet needs in MS management. The surveys were conducted at two international patient meetings in 2017 and 2018. Multiple answers were solicited in response to 10 questions.

Results: A total of 55 PwMS from Europe and 46 from North America completed the survey. PwMS in Europe listed a lack of time in medical appointments as their biggest challenge at diagnosis (60.0%) whereas, PwMS in North America reported understanding disease progression to be their biggest challenge (57.8%). European PwMS reported greater levels of additional patient support available in their clinics (i.e. MS nurse (67.3%), information about employment (21.2%), or psychological support (25.0%)) whereas, 26.1% of North American PwMS reported

no additional support. PwMS in Europe reported being less involved in treatment decisions with 20.5% saying they were not involved, compared with 2.4% in North America. European PwMS placed more importance on the safety of their treatment (57.7%) whereas PwMS in North America placed more importance on the efficacy of their treatment (71.7%).

Conclusions: There were distinct geographical variations between PwMS perceptions and priorities relating to MS care, education, and treatment decisions. European PwMS reported less time in appointments and lower involvement in treatment decisions than North American PwMS however, they also reported greater levels of support and education outside of their neurologist appointments including greater access to specialist MS nurses.

Disclosure: *Sarah A. Morrow: Biogen Idec, Novartis (contracted research). Celgene (consulting fee). EMD Serono, Roche, SanofiGenzyme (speakers bureau). Alexey Boyko: Biogen, Schering, Merck, TEVA, Novartis, Sanofi-Genzyme, Actelion, Biocad, Generium (consulting fee, participated in clinical trials supported by all above companies). Heidi Thompson: Biogen, Merck KGaA (consulting fee). Maija Pontaga: Merck KGaA (consulting fee). Nektaria Alexandri: Merck KGaA (salary).*

Keywords: Comprehensive care and MS, Shared-decision making

Methods of Care

(MOC01)

Understanding the HCP-Patient Relationship in Treating MS

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Background: HCPs play a critical role in treating MS patients, especially in helping patients get on treatment to help slow progression. An online survey of MS patients as well as natural language analysis of organic interactions on a social network provided insight into the relationship between HCPs and their MS patients. Understanding the HCP-patient dynamic is crucial to improving these interactions as well as identifying tools and educational materials to help patients better manage MS.

Objectives: Leverage MS patient social network to understand the HCP-patient dynamics, including what's working and any opportunities to improve HCP-patient interactions.

Methods: A two-pronged approach was undertaken. First, an online survey was completed by 658 US members of MyMSTeam in November 2018. Research was also conducted on de-identified organic discussions within MyMSTeam.com, social network of >127,000 people diagnosed with MS (approximately 1:9 MS patients in US). A Natural Language Processing tool (NLP) analyzed 178,884 verbatims April to September 2019.

Survey results showed 71% of patients indicated they rely on HCP for information about Disease Modifying Treatments (DMTs), 69% indicated HCP's recommendation to get on a specific DMT is most important factor, and 20% indicated decision to get on a DMT would be easier had HCP provided stronger opinion rather than relying on the patient to research and decide.

Results: analysis on doctor-patient relationship found 15% of conversations on MyMSTeam, n=37,978 discussions focused on HCP-patient relationship. 57% of conversations were generally negative in tone. NLP analysis revealed the dichotomy of the HCP-patient relationship. Sentiment was very positive when HCP addressed MS holistically as well as when patient felt HCP was truly listening to their needs and concerns. Conversations negative in sentiment were often result of feeling rushed, not being listened to or when the patient felt only MS progression was being addressed by HCP and not other symptoms also experienced.

Conclusions: Understanding the needs of MS patients provides significant opportunities for HCPs to better support and educate their patients, including through consultation that includes a stronger recommendation on treatment path as well as listening to patient concerns and addressing the sum total impact of MS including pain, depression and fatigue and not just disease progression.

Disclosure: *Beth Schneider: MyHealthTeams (contracted research).*

Keywords: Comprehensive care and MS, Management of activities of daily living in MS, Psychological issues and MS

(MOC02)

Cancelling Clinic Appointments: What Factors Are Associated with Higher Rates of Cancellations in Patients with Multiple Sclerosis?

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Background: It is important that persons with multiple sclerosis (MS) attend their scheduled appointments to maintain continuity of care and promote successful self-management. A recent study examined missed appointments in Veterans with MS and developed a model that included seven predictor variables (suboptimal disease modifying therapy [DMT] adherence (>80%), emergency visits, age, distance, and histories of post-traumatic stress disorder, chronic obstructive pulmonary disease, and congestive heart failure). However, to date, there is limited information on appointment cancellations, which is a different appointment attendance behavior but can also disrupt care.

Objectives: (1) To identify the rate of cancelled appointments in a large national sample of persons with MS and (2) to examine the demographic and clinical factors associated with high levels of cancelled appointments (defined as ≥50th percentile).

Methods: Administrative data between 01/01/2013 and 12/31/2015 were extracted from the VA MS Center of Excellence Data Repository, an electronic health record-based dataset composed of US Veterans receiving services at any Veterans Affairs (VA) medical center. The cancellation rate was calculated by dividing the number of cancelled appointments (excluding "no shows") by the total number of scheduled appointments during this two year timeframe. Bivariate analyses were conducted to examine demographic and clinical characteristic differences between individuals with and without high rates of cancellations, and variables with a p-value of <.10 were entered into a logistic regression.

Results: Over 96% (n=3,623) had at least one cancelled appointment, with a median cancellation rate of 25%. Flags for high rates of cancellations included one or more inpatient hospitalizations (odds ratio [OR]: 1.78), wheelchair issuance (OR: 1.48), distance (≥24.1 miles away; OR: 1.47), gender (male; OR: 1.28), suboptimal DMT adherence (OR: 1.26), and history of a mood disorder (OR: 1.28).

Conclusions: Cancelled appointments are prevalent among Veterans with MS. The similarities and differences in the variables included in the cancelled and missed appointment models highlight both malleable and non-malleable factors associated with each type of appointment attendance behavior. While further information is needed to elucidate the reasons behind these cancelled appointments, these results may help clinicians identify individuals at risk for higher rates of cancellations and to plan targeted interventions.

Disclosure: *Nothing to disclose.*

Keywords: appointment attendance, Comprehensive care and MS

(MOC03)

From Therapy Enrollment to First Dose - a Quality Improvement Initiative for MS Care

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Background:

Timely treatment is important for reducing relapses and risk of disability in people with multiple sclerosis (MS). However, disease-modifying medications entail a complex enrollment process that can delay treatment initiation.

Objectives:

This pilot study tracked individuals initiating the enrollment process for ocrelizumab and natalizumab at the University of Florida (UF) MS Clinic.

Methods:

This quality improvement initiative captured all relevant documents, including enrollment forms, insurance communications, referrals, and other documentation. We monitored the dates of completion, signature, fax, and local medical record upload for all forms.

Results:

Preliminary data from January 1, 2019 to October 1, 2019 captured 19 patients enrolled in either medication. Of these 19 patients, 6 received treatment as of October 2019. On average, enrollment submission to treatment initiation took 56 days, ranging 5-135 days. Of the remaining 13 awaiting treatment, the average interval from enrollment to October 2019 was 83 days, ranging 4-175 days. Overall, 11 quantifiable delays were identified, resulting in 17 recorded contacts. Of the 11 delays, 45.5% were insurance related, 36.4% were clerical delays, and 18.1% were patient related. Delays took an average 24.6 days to resolve (30.4 days, 9.25 days, and 41 days, respectively). For the 17-recorded contacts, 41% were insurance-related, 47% were clerical errors, and 12% were related to patient compliance. The majority of delays occurred in patients referred to outside infusion centers for treatment.

5 of 13 ocrelizumab patients initiated treatment as of October 2019. 4 of the 5 patients were infused at UF. The 8 patients awaiting treatment were referred to outside infusion centers and averaged 101 days without treatment as of October, 2019. 2 off 4 natalizumab patients have received treatment, both infused at UF. The 2 awaiting treatment, both were referred to outside infusion centers, and have waited an average of 71 days for treatment as of October 2019.

Conclusions:

Preliminary analysis suggest that insurance-related delays were the largest barrier to treatment initiation. Referring patients to outside centers further impeded the process. The results indicate that revisions to standard operating procedures for insurance inquiries and referrals may be beneficial. Moreover, while clerical errors were common, they were quickly resolved. Patient compliance issues, though rare, had the most enduring effect on treatment initiation.

Disclosure: *Jamie Bolling, Ryan McNiff, Tirisham V. Gyang, Carlos Vervloet Sollero: Nothing to disclose. Aaron Carlson: Novartis Pharmaceutical (contracted research). Sanofi Genzyme (consulting fee).*

Keywords: Comprehensive care and MS, Quality Improvement

(MOC04)

Nurse Telephone Encounters in an MS Clinic in 2020

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Background:

With the growing treatment landscape in multiple sclerosis (MS), nurses are being challenged with a constantly increasing work load, and more of their time is being spent on telephone encounters. Previous data collected from January to April, 2001 at the University of Calgary MS Clinic showed that 50% of nursing time was devoted to telephone encounters, and 30% of those encounters dealt with issues around disease modifying therapies (DMT's). In 2001 there were 3 Health Canada approved DMT options as compared to 12 approved DMT's at this time in 2020. Increased patient therapy choice has required more nursing time to educate patients on treatment expectations, potential adverse effects, and adherence to more complex medication protocols. There is a need to understand the type, frequency, and time spent on telephone encounters which will assist MS Nurses to develop efficient and effective management protocols.

Objectives:

To determine the frequency, type, and duration of nurse telephone encounters

To compare work previously done in the MS Clinic by Harris et al in 2001.

Methods:

Patient telephone encounters will be analyzed from January 2, 2020 to the end of March 2020. A telephone call log designed based on previous workload analysis at the University of Calgary MS Clinic will be utilized to capture the type, duration, and frequency of calls.

Results:

Telephone encounters are ongoing, with data analysis completed April 1, 2020.

Conclusions:

Analyzing telephone encounters will provide information to assist with the development of work load management strategies.

Disclosure: *Janice Lake: senofi Genzyme (consulting fee). Colleen Harris: Biogen, Merck Serono, Novartis, Roche, Sanofi Genzyme (consulting fee). Sharon Peters, Jackie Gaythorpe: Nothing to disclose.*

Keywords: Comprehensive care and MS

(MOC05)

Pioneering MS Center Program with MSHA Certification to Improve Patient Care and Experience

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Background:

The OSF HealthCare Illinois Neurological Institute's Multiple Sclerosis Center is a Certified Comprehensive MS Center located in Peoria, Illinois, serving over 2,100 patients and is focused on providing excellence in multiple sclerosis care for patients and families in need through diagnosis, treatment, education, and research.

Like many MS Centers we are fortunate to have physicians, nurses, physical therapists, occupational therapists, and a registered dietician who are specialized in multiple sclerosis. However, we came to realize there were opportunities in our level of patient care and experience with the potential to be transformed if we invested in our Medical Office Assistants and our MS Patient Navigators through MSHA Certification. Certified employees are able to deliver a higher level of care, better connect patients to resources, and also better support our comprehensive care team, which allows our center to ensure all members are working at the height of their licensure. We set a goal in May of 2019 to have a mission partner in every job role of our MS Center to be certified in multiple sclerosis. We propose that achieving this level of certification in each and every MS Center around the world is a goal worth aspiring toward in our combined fight for MS.

Objectives:

MSHA Certification within our Medical Office Assistant and MS Patient Navigator job roles in 2019. In addition, lower risks associated with delay of treatment, removing barriers to

care, increasing clinical competency, and employee efficiency in tasks such as prior authorizations for disease modifying therapies.

Methods:

Investing in team study and elevating employees through MSHA Certification. We also brought our team to CMSC for education, networking, and patient resource opportunities.

Results:

The OSF HealthCare Illinois Neurological Institute's MS Center has an employee in every job role who is MS Certified. MSHA Certification has given our team members greater context and compassion through a deeper understanding of multiple sclerosis at a professional level. We increased efficiency and decreased delay in care and also the time it took to obtain prior authorizations. Our certified employees are able to communicate with an increased level of empathy and confidence with patients. MSHA Certification has fostered career dedication and driven passion while motivating our MS care team as a whole.

Conclusions:

MS is a complex and lifelong neurological disease that requires all individuals involved with patient care to have a basic level of knowledge of the disease. The MSHA Certification of our employees is a pioneering strategy that has elevated the level of care and experience we provide to our patients living with MS by empowering our employees through the education and understanding of multiple sclerosis. MSHA Certification is an effective tool for efficient and empathetic healthcare delivery to those individuals living with multiple sclerosis.

Disclosure: *Nothing to disclose.*

Keywords: Comprehensive care and MS, MSHA Certification

(MOC06)

Conceptualizing Access through the Perspectives of Canadians with MS

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Background:

Access to healthcare is vital to the health and well-being of people with chronic conditions like MS. Access is often measured using service utilization as a proxy. Utilization measures may fail

to capture the complexities of the experiences of accessing care that populations with chronic illness face. The Candidacy Framework offers an alternative to utilization measures, by examining the dynamic process a patient must engage in, with the healthcare system and all components of it, to negotiate their eligibility for care, which is described as one's candidacy. The process of accessing care is examined form the perspective of vulnerable populations and considers the impact of social patterning and health system environments on this process.

Objectives:

To investigate access to healthcare for the management of MS, in a Canadian context, from the perspective of Persons with MS.

Methods:

The study design was informed by an interpretive descriptive methodology. Forty-eight individuals with MS living across seven communities in Ontario were recruited primarily through the MS Society of Canada to participate in one of five focus groups or ten individual telephone interviews. The sessions were digitally recorded and transcribed. The transcriptions were then analyzed using constant comparative methods. Additionally, the data was re-interpreted in light of the Candidacy Framework to determine its alignment to this framework.

Results: All dimensions of the Candidacy framework were relevant to the experiences of persons with MS. However, the framework failed to account for important aspects of the participants life-long experience of accessing care. Importantly, participants discussed the process of engaging in help-seeking which was informed by past experiences of seeking and receiving healthcare services, as well as the accumulated knowledge of living with MS. The most commonly reported past experiences were those regarding instances of patient centered care, where negative experiences were described when this approach to care was not taken. Past negative experiences oftentimes made persons with MS hesitant to seek further care.

Conclusions:

The Candidacy Framework alone does not account for the lifelong interaction with healthcare that individuals with chronic illnesses such as MS face. To capture the full experience of access the framework should consider three main extensions: (1) The addition of recursivity, which captures the reciprocal nature of interacting with the healthcare system; (2) Inclusion of help-seeking behavior and related decision making and; (3) Inclusion of the concepts of patient-centered care.

Disclosure: *Nothing to disclose.*

Keywords: Access to Healthcare , Comprehensive care and MS

(MOC07)

Access to Healthcare for Canadians with MS: Prioritizing Concerns

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Background: Current Canadian literature demonstrates that persons with MS are high users of healthcare services, yet still have multiple unmet needs and low satisfaction with healthcare services. International studies showing similar results suggest this may be related to issues in access to healthcare.

Objectives: We aimed 1) to describe the healthcare service use of Canadians with MS in managing their condition; 2) to identify the most pressing concerns Canadians with MS have in relation to accessing care to manage their MS.

Methods: The aims were addressed using an online cross-sectional survey guided by Concerns Report Methodology. Inclusion criteria were: over 18 years of age; a Canadian Citizen, and self-reported diagnosed of MS. Data were collected about healthcare service use and the importance and satisfaction with access to healthcare service in the community. Data were analyzed using descriptive statistics. Access concerns were prioritized by calculating a Needs Index (NI).

Results: To date, 211 persons with MS have completed the survey. Participants were predominantly female (86%), with a mean age of 46.4 (standard deviation (SD)=11.7), living with relapsing remitting MS (77%) for a mean of 10.4 years (SD: 8.9). Just over half of the participants were still working (57%), with varying levels of disability ranging from 0-7 on the Patient Determined Disease Steps (Median: 2). Preliminary findings indicate that nearly all participants had a regular neurologist (97%), many of which practice in an MS clinic (83%). Most individuals also had a general practitioner (96%). Participants on average visited their neurologist 1.5 times a year (SD:0.7) and their general practitioner 4.6 times (SD:2.3) a year. The highest concerns among participants regarding their access to care were: 1) affordability of complementary care (example: massage therapy, yoga, naturopathic care) (NI: 33.8) and physiotherapy and occupational therapy (NI: 29.7), both aimed at improving wellness; 2) availability of healthcare providers with MS-related knowledge in their communities to guide their care plan (NI: 33.7); and 3) communication between healthcare providers to ensure coordination of care (NI:29.2).

Conclusions: Preliminary findings suggest that for persons with MS, merely having a regular neurologists and general practitioners is not considered satisfactory access to care. Persons with MS identified concerns regarding the availability of affordable healthcare services aimed at maintaining wellness. They also had concerns regarding the availability of community providers with sufficient MS-related knowledge to guide their referrals and care plans. Targeting policy

reform promoting the coverage of healthcare services aimed at preventative and maintenance care may be a critical step in improving care for this population.

Disclosure: *Nothing to disclose.*

Keywords: Access to Healthcare, Comprehensive care and MS

(MOC08)

Use of a Clinical Decision Support Tool to Support Monitoring and Care of Patients with Multiple Sclerosis Receiving Disease Modifying Therapy

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Background: As the number of FDA approved disease modifying therapies (DMTs) utilized to treat various forms of multiple sclerosis (MS) increases, the monitoring requirements for DMTs also increases. The use of the TheraDoc® software program, a clinical decision support tool (DST), has been shown to improve patient care, comply with guidelines of care, optimize cost of care, create efficiencies of care and minimize adverse drug events.

Objectives: To compare the delay to treatment and monitoring using manual vs. automated surveillance.
To compare the time to manually enter data vs. automated data for case management
To highlight medication adherence

Methods: Theradoc® has been utilized for case management in a variety of medical settings in the VA healthcare system; it has not been utilized for the care of patients with MS. A dashboard of MS patients who are prescribed a DMT was developed with consideration of the VA criteria for use (CFU) guidelines. Features include automation of lab results, flag reports, real time alerts, team communication, ability to export report and various views of the dashboard. Theradoc® is linked to the VA's computerized patient record system and is currently being piloted at 3 sites.

Results: The features of the Theradoc® MS DMT software program will be reviewed in a series of interactive figures. We assessed the experience of 120 patients (at present) with MS utilizing various DMT modalities. Demographic and clinical characteristics of all patients will be summarized. Outcomes including patient adherence, time to assess and order lab assessments and follow-up with patients will be contrasted between the manual and automated surveillance groups. Errors in making assessment will be noted. Data will be analyzed and we anticipate a decrease in delay to treatment, improved compliance with monitoring as established by the CFU

guidelines with the use of Theradoc® clinical DST and case management. Overall time efficiency will be contrasted between the manual and automated surveillance approaches.

Conclusions: Using a clinical DST linked with an electronic health record providing the MS clinical team with required data improves MS DMT monitoring and decreases risk for adverse drug events of patients who receive DMT and improves MS team communication

Disclosure: *Nothing to disclose.*

Keywords: Comprehensive care and MS, Disease-modifying treatments in MS, Nursing management in MS

(MOC09)

Multiple Sclerosis Disease Impact Monitoring: Longitudinal Exploration of the Relationship of OCT to Computerized Cognitive Testing

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Background: Disease impact and change in routine care for people with Multiple Sclerosis (PwMS) is typically measured by combining EDSS, MRI change, and reported relapse. Cognitive impact can be objectively tracked with digital cognitive assessment batteries (CAB) and retinal nerve fiber layer (RNFL) density (Ocular Coherence Tomography, (OCT)). Cognitive and RNLF impact are not quantified by traditional care approach (EDSS, MRI, Relapse). Enhancing shared decision making to optimize PwMS treatment selection could be accomplished by incorporating quantitative measures that provide objective examiner independent information reflecting disease impact and possibly differentiating relapse from progression. Utilization of the NeuroTrax CAB to measure a global cognitive summary score (GCS) based on seven tested domains (memory, executive function, visual spatial, verbal function, attention, information processing, motor skills) combined with OCT RNFL measures could lead to earlier detection of disease activity as well as assisting in optimal treatment selection.

Objectives: To explore the relationship between rate of change in PwMS seen in both a global CAB score and various OCT measurements.

Methods: Retrospective chart review of CAB and OCT scores collected in the process of routine care. Paired sample T-tests were done between percent change of 2 visits, 1 year apart, with GCS

and the following OCT measurements (right OD and left OS eyes): RNFL (sublayers: Global (G), Nasal/Temporal ratio (N/T)), papillomacular bundle (PMB), macular volume (MV).

Results: N=103 75% female, average age at first visit 51±10. All regressions run between CAB-GCS and OCT measures yielded p values >.05 at both visit 1 and visit 2, save for the CAB-GCS G-OS relationship. A significant difference was not observed (p>.05) in the percent change between visit 1 and 2 when comparing the following OCT measurements with the CAB GCS: G-OD&OS, N/T-OS, PMB-OS, MV-OD&OS. Significance was observed (p<.05) of: N/T-OD and PMB-OD.

Conclusions: The relationships of global RNFL densities to global CAB scores remained the same after a year, which suggests that both measures identify disease change in a synchronous manner in monitoring PwMS disease progression. Non-significance between percent changes suggests that OCT and cognitive scores change at similar rates at least within a year's period of time. A larger longitudinal study is suggested to further determine the relationship between OCT and cognitive changes over greater lengths of time.

Disclosure: *Mark Gudesblatt: Acorda, Amgen, Biogen, EMD Serono, Medtronic, Novartis, Sanofi, Saol Therapeutics, Teva (consulting fee). Biogen, EMD Serono, Novartis, Sanofi, Teva (contracted research). Jared Srinivasan, Olivia Kaczmarek, Daniel Golan, Timothy Fratto: Nothing to disclose. Glen Doniger: NeuroTrax (salary). Jeffrey Wilken: Biogen (contracted research). EMD Serono (speakers bureau). Genzyme (contracted research, speakers bureau). Robert C. Sergott: Biogen Idec; Clene Nanomedicine; Heidelberg Engineering GmbH; Janssen Global Services, LLC; Medtronic; and Merck & Co., Inc (consulting fee). Biogen Idec; Clene Nanomedicine; Janssen Global Services, LLC; Medtronic; Nightstar; and ThromboGenics NV (contracted research). Biogen Idec; Genzyme Corporation; Novartis Pharmaceuticals Corporation; and Teva Pharmaceutical Industries, Ltd (speakers bureau).*

Keywords: Comprehensive care and MS, Equipment in MS, Natural history of MS

(MOC11)

Improving Understanding of Clinical Phenotype for Patients with Multiple Sclerosis: Design and Implementation of Smarttools in Electronic Health Record Systems

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Background: Patients with multiple sclerosis (MS) frequently require complex clinical care and decision making, including monitoring for relapses, chronic immunosuppressive therapy, and extensive serological and imaging work-up. Modern electronic health record (EHR) systems offer the opportunity to facilitate understanding of each patient's clinical phenotype by allowing discrete data collection, as well as summarization and presentation of critical information to

providers. However, such tools often require custom design and build, for which many institutions do not have assigned resources.

Objectives: To implement a comprehensive set of EHR-based Smarttools for MS patients that can be shared among institutions to improve data quality and understanding of patient phenotype.

Methods: The Epic EHR system was used to develop several Smarttools. A Smartform was designed to allow discrete data collection on items considered critical by MS experts. Content included date of diagnosis, documentation of relapse characteristics, such as date, duration and therapies, current and past immunosuppressive therapy, critical imaging and results of CSF studies. Longitudinal caption of disease impact was incorporated, including number of falls and ability to walk since last visit. Logic was applied to conditionally display the SmartForm for patients with a diagnosis of MS. A synopsis was designed to visualize longitudinal data, and a SmartPhrase was implemented to automate documentation of discrete data in provider notes.

Results: Version 1 of the MS Smartform was implemented in August 2017. Over the course of 18 months, data on approximately 1000 unique patients were collected. The SmartForm was found to be easily accessible and easy to navigate by providers and the completion rate was high. Based on the initial experience, version 2 of the Smartform was designed and was recently implemented with minor modifications to minimize erroneous data collection, and a predefined list of immunomodulatory therapies and more detailed information about reasons for starting and stopping therapies was included. Data entry for the full cohort of ~3000 patients is ongoing. With the support of the Epic Neurology Steering Board, all discrete data elements were incorporated into the Epic Foundation system to facilitate implementation of the Smartform at other institutions.

Conclusions: EHR systems provide opportunities to improve understanding of complex clinical phenotype. We built a comprehensive Smartform that facilitates discrete data collection and review for patients with MS. This tool is being made available in the Epic Community library and can be implemented without charge at other institutions. Besides offering a better understanding for individual patients, it is our hope that this SmartForm will contribute to better streamlining of data collection across institutions and ultimately, better outcomes for patient care and collaborative research.

Disclosure: *Thomas Grader-Beck: Abbvie, Celgene (contracted research). Lilly (consulting fee). Yujie Wang, Kathryn C. Fitzgerald: Nothing to disclose. Peter A. Calabresi: Biogen and Disarm Therapeutics (consulting fee). Ellen M. Mowry: Biogen, Sanofi, Genzyme (contracted research). Biogen, Sun Pharma (site pi). Teva (pi clinical trial). UpToDate (royalty).*

Keywords: Comprehensive care and MS, Electronic Health Record

(MOC12)

Changing Language to Acknowledging Patients Perceptions of Treatment in MS Care

Tim O'Maley
Nursing, MS Queensland, Brisbane, QLD, Australia
Background: None

Objectives: None

Methods: None

Results: None

Conclusions: None

The language we use in supporting our patients is crucial in fostering a long term relationship based on trust and understanding. However, it is important to remember that information does not equal education, and the ability to make the complexities of medicine comprehensible for patients is an important skill. Two recently published papers of almost opposing direction have highlighted the message that "I" can do better.

Yeandle et al strongly emphasised the increased role patients and their families have in shared decisions making, noting "its success is reliant on effective patient–physician communication". Burke et al in their paper on management of surplus suffering discuss how HCPs can negatively impact the perception of the disease and recognising our control of information sharing may "go a long way to improving clinical encounters with patients and ultimately lead to greater satisfaction in care and shared decision making".

This presentation will briefly explore the core concepts of recent literature that have resulted in a shift in language used by the author in delivery of both clinical patient care and group educational opportunities, and the qualitative patient responses that emphasise the value of patient centricity in MS care.

Disclosure: *Tim O'Maley: Biogen, Novartis, Roche (consulting fee).*

Keywords: Comprehensive care and MS, Disease-modifying treatments in MS, Nursing management in MS

Neuroimmunology and Disease Models

(NDM01)

Efficacy of the Influenza Vaccine in Multiple Sclerosis Patients: A Systematic Review and Meta-Analysis

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Background: Multiple sclerosis (MS) is a neurodegenerative disease thought to be of autoimmune origin[1]. It leads to the development of neurological symptoms and increases the risk of infection from communicable diseases[1,2]. Thus, vaccines are endorsed to mitigate this risk. However, it has not yet been confirmed whether these patients' dysfunctional immune system combined with taking immunosuppressants can lead to a dampened immune response against the influenza vaccine[2]. Infection with the influenza virus is a concern for MS patients[2]. Previous research on MS patients who have received the influenza vaccine focuses on safety and relapse rates.[3] Studies that focus on the immune response mounted against the vaccine in these patients are scant.

Objectives: This study serves to compile this previous research in order to provide a comprehensive picture of the efficacy of the influenza vaccine in MS patients

Methods: This was done through a systematic review and meta-analysis.

Results: The results of this study suggest that MS patients can mount an adequate immune response to the influenza vaccine when compared to healthy controls. Most of the immunotherapies these patients are on do not appear to affect this immune response.

Conclusions: Therefore, the influenza vaccine should continue to be recommended to MS patients.

Disclosure: *Nothing to disclose.*

Keywords: Comprehensive care and MS, Immunology and MS, Vaccination in MS

Non-imaging Biomarkers

(NIB01)

Higher Sensitivity of Quantitative RT-PCR Compared with Flow Cytometry for Quantification of B Cells after Anti-CD20 Monoclonal Antibody Therapy

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Background: Preclinical and clinical evidence have shown promising results for CD20+ B-cell-target-based therapies in multiple sclerosis (MS). Ofatumumab, a fully human anti-CD20 monoclonal antibody (mAb), depletes circulating peripheral B cells and is in Phase 3 development for relapsing MS.

Objectives: Compare sensitivity of reverse-transcriptase polymerase chain reaction (RT-PCR) and current standard fluorescence-activated cell sorting (FACS) for quantification of CD20+ B-cell depletion.

Methods: Raji B cells, stained with anti-CD19-FITC (HIB19) and anti-CD20-PE (2H7), were spiked at 12 dilutions (0.3-100 000 cells) into 100 000 THP-1 cells (CD19-/20-); each sample was split for FACS and RT-PCR. Absolute counting beads (Invitrogen) were used to define minimal FACS detection level of CD19+/20+ cells by BD Fortessa (stopping gate fixed at 2000 beads). Limit of detection (LoD) and limit of blank (LoB) were determined as per international guidelines. For RT-PCR, total RNA was extracted (RNeasy Mini kit). Duplex TaqMan assay with CD19-VIC (Hs00174333m1) and CD20-FAM (Hs00544818m1) probes was run in quintuplicate, after reverse transcription (SuperScript III). Copy numbers were determined via a standard curve from serial dilutions of linearized quantified plasmid of CD19/CD20 target sequences. PCR reactions were set up by an Echo 525 acoustic liquid handler with a total volume of 2.5 µL.

Results: An LoB of 70 cells and LoD of 90 Raji cells spiked into 100 000 THP1 were observed by FACS with no difference between CD19+ and CD20+ cells. A reliable correlation between spiked and bead-extrapolated counts of approximately 300 cells was observed. Sensitivity of RT-PCR was assessed similarly; efficiency for both TaqMan assays was >98% with LoD of 2 copies of mRNA. On average, Raji cells expressed 15-20 copies of CD19 and 60-100 copies of CD20 transcripts per cell. A reliable correlation was seen for CD19 and CD20 down to 10 spiked cells.

Conclusions: Quantification of total B cells in blood and tissue after anti-CD20 mAb treatment by sensitive and specific RT-PCR seems feasible. In addition to simpler sample logistics, this method can measure CD20 gene expression directly.

Disclosure: *Ismahane Touil Allaoui, Marija Colic, Friedrich Raulf, Gisbert Weckbecker: Novartis Pharma AG (salary). David Leppert: Novartis Pharma AG (former employee).*

Keywords: Disease-modifying treatments in MS, Immunology and MS

(NIB02)

Quantification of Smooth Pursuit Dysfunction in MS

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Background: A significant proportion of MS patients have efferent visual system dysfunction that may impair ability to read or work or lead to dizziness, gait impairment or falls. Quantifying oculomotor deficits also offers promise as a biomarker of MS disease burden.

Objectives: The purpose of this study is to use a novel non-invasive NASA-developed eye tracker (neuroFit ONE) to detect and quantify abnormalities in oculomotor function in MS patients vs. healthy controls.

Methods: We recruited consecutive subjects from the UCSD MS clinic who met the 2017 published MS criteria and healthy controls without any history of neurological disease, head trauma or other source of afferent/efferent visual deficit. The neuroFit ONE eye tracker was used to measure latencies, acceleration, gain, saccadic correction amplitudes, proportion of smooth vs. saccadic eye movements, direction tuning and speed tuning in MS participants vs. healthy controls. Each test was repeated 3 times to assess reproducibility and to generate a mean value. A composite of the individual tests was generated (nfit). Comparisons of the oculometrics with case status were assessed by regression methods.

Results: Ten patients with MS and 17 healthy controls have been enrolled to date. The mean overall composite score of oculomotor function (nfit score) was worse in MS patients vs. controls (-1.6, 95% CI -2.9, -0.20, p=0.026). Mean latency for initiating smooth pursuit was 6 ms longer for MS participants (95% CI 0.65, 12.6, p=0.031). There was decreased mean initial acceleration of eye movements (-37.2, 95%CI -67.6, -6.9, p=0.018) in the MS eyes. The proportion of smooth vs saccadic eye movement was lower in MS eyes (-16%, 95%CI -30%, -23%, p=0.0.24). The additional metrics measured showed similar patterns.

Conclusions: We were able to comprehensively capture and quantify oculomotor dysfunction in MS participants compared to controls, including aspects of smooth pursuit that have not previously been well quantified in MS.

Disclosure: *Neda Dastgheyb, Miryam Palomino, Annalise Miner: Nothing to disclose. Revere P. Kinkel: Biogen (speakers bureau). Dorion Liston: neuroFit (founder). Jennifer S. Graves: Biogen, Octave, and Genentech (research support). Novartis, Genentech, Alexion, and Celgene (consulting fee).*

Keywords: neuro-ophthalmology

Neurophysiology; Neuropsychology and Neuropsychiatry

(NNN02)

Education As a Moderating Variable in the Relationship between Patient Self-Perception of Cognitive Impairment and Sdmt Performance in MS

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Background: Approximately 40-60% of patients living with Multiple Sclerosis (MS) experience some degree of cognitive impairment. Available evidence suggests greater education level serves as a protective factor and is related to cognitive reserve and premorbid intelligence. Individuals with higher levels of education may be differentially impacted by reduced processing speed, when compared to those with lower levels of education. Alternatively, there may be differences in degree of awareness of cognitive deficits as a result of educational attainment. Numerous studies signal the importance of early detection in cognitive impairment in overall MS disease burden and treatment outcomes. However, many clinicians rely on patient self-report in determining whether to refer a patient for in-depth cognitive testing. It can be difficult for clinicians to accurately gauge cognitive impairments during brief clinical visits, and certain factors may impact how patient self-report is interpreted (i.e., education level, cognitive reserve). Recent standard of care guidelines have been published which outline the utility of the Symbol Digit Modalities Test (SDMT) as an early screening measure to be used to establish baseline cognitive functioning[5].

Objectives: The current study (N=75) evaluated whether education level moderated the association between SDMT scores and patient self-report of cognitive dysfunction.

Methods: Patient self-report of cognitive dysfunction was evaluated via EMR review of neurology consult notes. All patients were administered the SDMT after their neurology consult visit, and highest level of educational attainment was obtained via self-report.

Results: Linear regression modeling compared SDMT scores of those who endorsed cognitive symptoms (n=22; M=-1.09, SD=1.1) to those who did not (n=53; M=-.19, SD=1.16). Results showed a significant difference in model 1, $F(1, 72) = 9.4$, $p=0.003$, indicating that those who endorsed cognitive deficits yielded lower SDMT scores. Model 2 did not support education in moderating this effect.

Conclusions: While patient self-perception did correlate with SDMT performance, level of education of the patient did not impact this relationship.

Disclosure: *Elizabeth Kera, William A. Tsang, Nina A. Curko, Lee S. Ifhar: Nothing to disclose. Florian Thomas: Genentech, Novartis, Sanofi (speakers bureau). Krupa Pandey: Alexion, Biogen, Genentech, Novartis, Sanofi (speaker/consulting).*

Keywords: Comprehensive care and MS, Management of activities of daily living in MS, Neuropsychology

(NNN03)

Preliminary Cognitive Outcomes Following Mesenchymal Stem Cell Therapy in Multiple Sclerosis

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Background: Mesenchymal stem cells (MSCs) are being investigated as an alternative disease-modifying therapy for multiple sclerosis (MS) given their immunomodulatory and tissue repair properties. MSCs are multipotent progenitor cells that can differentiate into mesodermal cells with neuroprotective and pro-oligodendrogenic properties. Little is known about potential effects on cognition.

Objectives: To evaluate cognition following MSC therapy over 48 weeks.

Methods: 28 individuals with inflammatory MS (17 RRMS, 7 SPMS, 4 PPMS) were enrolled in a randomized, double-blind, sham-controlled cross-over study of autologous MSC with the primary outcome determined at 24 weeks. Participants were randomized to receive either a single IV infusion of MSC or a sham infusion at week 0, then crossed-over at 24 weeks to the alternate treatment arm for a further 24 weeks of observation. Participants underwent a comprehensive neuropsychological battery at weeks 0, 24 and 48. Cognitive domains assessed included: attention/information processing speed, language, visual perception, learning, memory, and executive functioning. To account for potential practice effects associated with serial testing, data were analyzed using reliable change analyses at the individual level. Performance on any given cognitive task was considered improved or declined if most of those who demonstrated change (at least 3 or more) obtained significant RCI values (±1.64).

Results: Participants were 15 females/13 males (EDSS 4.27 (1.25), age 37.36 (5.21) yrs, education 13.64 (1.61) yrs). Immediately after treatment, relative stability was noted for most cognitive tasks. Nonetheless, some change was detected. Decline was observed in some aspects of attention/information processing speed, visual learning and memory, as well as language. Improvement was noted in verbal learning and memory, as well as visual perception. In the early treatment group, where longer-term follow-up was possible, there was a trend for performance to

return to pre-treatment baseline, with the exception of visual learning and memory, which remained below baseline levels.

Conclusions: Except for visual learning and memory there appears to be little detrimental effect of MSC therapy on cognition. While some changes may occur in the initial period following treatment, these appear to be transient and, in general, return to baseline over time.

Acknowledgements: Funded in part by the MS Scientific Research Foundation and Research Manitoba

Disclosure: *Nothing to disclose.*

Keywords: CNS repair, Cognition in MS, Disease-modifying treatments in MS

(NNN04)

Relationship between EDSS Scoring and Attention Performance in People with Multiple Sclerosis

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Background: Multiple sclerosis (MS) is a degenerative, autoimmune and chronic neurological pathology. In addition to the symptoms of spasticity, fatigue, muscle weakness, numbness, urinary incontinence, among others, complaint of attention performance difficulty is very common. The Expanded Disability Status Scale (EDSS) is a method of quantifying disability in MS people, which is scored from 0 to 10. The higher the scoring, the greater the person's functional disability.

Objectives: To verify and analyze the relationship between EDSS scoring and attention performance in people with MS.

Methods: A quantitative study was performed with 41 people diagnosed with relapsing-remitting multiple sclerosis (RRMS), aged between 23 and 58 years (Mean = 42.70, SD=10.62 years), 14 men (34.1%) and 27 women (65.9%), with EDSS score from 0 to 6.5 and time of diagnostic between 1 and 26 years (Mean = 10.09, SD=6.67 years). For evaluation, an interview was conducted to collect data and a battery of neuropsychological attention tests was applied to each patient. The SPSS software was used for data analysis.

Results: It was observed that 20 patients (48.8%) presented alteration of sustained attention, 29 patients (70.7%) presented alteration of alternating attention and 27 patients (65.9%) presented

alteration of divided attention. There was a negative association between EDSS scoring and sustained attention performance ($p < 0.0001$) and alternating attention performance ($p = 0.037$). That is, the higher the EDSS scoring, the worse the performance of sustained and alternating attention. There was no significant association between EDSS scoring and divided attention performance ($p = 0.094$).

Conclusions: It is suggested from the results of this study that the level of disability status may affect sustained and alternating attention performance of people with MS.

Disclosure: *Nothing to disclose.*

Keywords: Multiple sclerosis, EDSS, neurological disease, neuropsychology, Psychological issues and MS

(NNN05)

Objective Measurement of Cognitive Impairment in Multiple Sclerosis Patients Using Novel Computerized Testing

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Background: Cognivue® is an FDA-cleared computerized testing tool rooted in adaptive psychophysics and designed to assess early signs of cognitive impairment (CI). CI has a substantial impact on productivity and quality of life in patients with MS, but testing has been limited. A brief, easy-to-administer neuropsychological test could increase the frequency of routine assessment of cognitive impairment among patients with MS, leading to a positive impact on MS management.

Objectives: At the completion of this presentation, participants should be able to assess the reliability of Cognivue® as a cognitive assessment tool in multiple sclerosis (MS).

Methods: The study was conducted at the University of Massachusetts Medical School between June 2016 and May 2017, and enrolled consecutive patients who consented to testing. Study participants completed the Expanded Disability Status Scale (EDSS), symbol digit modality test (SDMT), 9 hole peg test, timed 25-foot walk, and 10-minute Cognivue® testing (basic motor & visual ability, perceptual processing, and memory processing). Statistical analyses using a one-way ANOVA were performed to determine differences between neuropsychological testing methods.

Results: Thirty-six patients (mean age 48.6 y [range 20-74], 78% female [n=28/36]), completed the various tests. Based on Cognivue® scores, 50% of patients were categorized as having normal

cognitive function (mean 84.7; EDSS 2.64), 33.3% as having low to moderate CI (mean 66.0; EDSS 3.38), and 16.7% as having severe CI (mean 39.2; EDSS 5.17). Overall Cognivue® scores demonstrated statistically significant correlations with EDSS (Pearson correlation coefficient -0.54), SDMT (0.67), and timed 25-foot walk (-0.56). No relationship was seen between patient age and Cognivue® scores. All key cognitive domains were equally affected.

Conclusions: Cognivue® is beneficial in detecting early stages of multi-domain CI in MS patients providing a potential opportunity for early intervention strategies to improve patient outcomes.

Disclosure: *Roberto Bomprezzi, Kerime Ararat: Nothing to disclose. Kara Smith: Acorda (served on expert panel). Reina Benabou: Cognivue, Inc. (i am cognivue's cmo).*

Keywords: Neuropsychology, Cognition

Programs

(PGM01)

The Use of an MS Documentary Film Screening Program As an Educational Intervention to Increase Knowledge and Awareness about MS and Support Resources

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Background: Typical MS educational methods include brochures, handouts, community presentations, or on-line resources. First-person experiences living with illness are common ways to learn about health conditions. Film is a non-threatening modality to increase knowledge and awareness about MS and its impact.

Objectives: Increase MS knowledge and awareness via documentary film screening "*When I Walk";* Increase awareness of local MS resources.

Methods: Study approved by UNC Charlotte IRB. This post-test only study included 68 participants who attended an evening MS film documentary screening event in November 2019. "*When I Walk,* is the first film in a trilogy of films about MS. The second film, "*When We Walk*" premiered in 2019, and the third film, "*When They Walk*" is in production. 45 participants completed an online event survey.

Participants ranged in age from 18 years to 74 years old and the majority were female (79.1%; n=35). Just over half of the participants were Caucasian (n=27); 7 Black or African-American

and were well-educated with university degrees.The film screening was delivered by a social work researcher and health services doctoral student and shown in a 600 person auditorium. A slideshow with information about the film, panelist bios, vendors, and follow-up MS film and educational events scrolled before and immediately after the film screening. A panel discussion including five participants immediately followed the film screening: local National MS Society representative, university ADA director, a physician's assistant specializing in neurology, one person living with MS, and one person living with MS who is also a healthcare professional and support group facilitator.

Results: Results suggest an overwhelmingly positive and enthusiastic outcome and impact on participants as a way to increase knowledge and awareness about MS and available resources. For example, 35 participants rated the MS film screening experience as "*excellent*" 41 participants "*strongly agreed' or "agreed*" that participation in the MS documentary screening increased their knowledge of MS and its related symptomatology; 36 participants "*strongly agreed*" or "*agreed*" that participation in the MS film screening increased their knowledge of available resources at UNC Charlotte and the surrounding area and 41 participants (95%) stated that the film screening helped them to better understand the social and cultural views of others who have had different life experiences.

Conclusions: Participant responses support using film documentary as an effective, creative, and friendly intervention to increase knowledge and awareness about MS and available resources and to increase collaborative partnerships between the university and community partners. Few examples exist in the literature about using film as an educational learning tool to educate persons about physical illness. There are several study limitations to consider in future events.

Disclosure: *Nothing to disclose.*

Keywords: MS and the caregiver/family, Psychological issues and MS

(PGM03)

Dance for a MS: A Structured Dance Program Targeted for Multiple Sclerosis Patients

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Background:

Multiple Sclerosis (MS) is a demyelinating disease of the central nervous system and a leading cause of disability. It presents multiple symptoms such as ataxia, weakness and fatigue, impairing independence and quality of life. Though advances have been made in preventing disability, pharmacological approaches to reverse it are not available.

The best tool for functional recovery in MS is rehabilitation, typically physical and occupational therapies. Exercise therapies provide symptomatic benefit and are widely used in rehabilitation protocols. In Parkinson's disease, different dance regimens have been shown to improve functional outcomes and to be superior to traditional exercise programs. Encouraged by this, we developed a structured dance class for MS, with specific targets, such as balance and exercise tolerance. The protocol was a collaboration of dance faculty, neurologists, physical and occupational therapists.

Objectives:

To present the University of Florida's "Dance for MS" – a dance program for symptomatic improvement and quality of life

Methods:

Classes occur weekly, with 75 minutes duration. They are taught by faculty from UF Center for Arts in Medicine and UF Health Shands Arts in Medicine, with an artist in residence. They start with a 15-minute seated warm-up, 15-minute barre exercise, 5-minute break, 15-minute center or across-the -floor section, 20-minute improvisation/dance composition and a 5-minute cool down. Classes combine elements of modern dance, ballet, jazz and social dance.

Results:

Classes launched in August 2018. Three to six people with MS attended each class, as well as one to three caregivers. In the past 18 months, the class performed interactive dances in community events such as the National MS Society Walk, HealthStreet's Night of Dance, and the Harn Museum's Museum Nights. While participant population is small, retention rate is high. Participants have reported improved balance, body awareness and confidence in their movement. They have also appreciated the accessible approach to dance, and their enjoyment of the class.

Conclusions:

The Dance for MS program presents a feasible rehabilitation strategy for patients with MS, with a targeted approach to common symptoms in this population. It is presented in a social and ludic format, which may be beneficial for affective symptoms. Similar dance programs can be

implemented as complimentary rehabilitation strategies. Formal trials to measure the impact of the dance program are needed.

Disclosure: *Nothing to disclose.*

Keywords: Complementary/alternative therapies in MS, Comprehensive care and MS

(PGM04)

Development of an Effective Age-Span Program for Women with Multiple Sclerosis: A Patient Perspective

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Background:

Multiple sclerosis (MS) is a chronic, life-long, unpredictable and potentially highly debilitating neurological condition which occurs more commonly in women than in men. It strikes most often in young adulthood, but can even start in childhood and adolescence. Young girls and adolescents with pediatric-onset MS, as well as adult women, often find it intimidating and overwhelming to navigate the complexities of the health care system. Typical MS programs may not focus on managing the impact of MS on puberty, fertility, pregnancy, the post-partum period, breastfeeding and menopause.

Objectives:

In order to develop a Comprehensive Age-Span Program for Women with MS at the Children's Hospital of Philadelphia (CHOP) and the Hospital of the University of Pennsylvania (HUP), health care providers must identify the health care needs from the patients' perspective. The population includes women with MS at every age, from teenager to older adult.

The purpose of this qualitative study will be to identify personal and health care needs of women with MS of all ages. The ultimate goal will be to provide patients and their families with high-quality education about their condition and establish a multi-disciplinary team approach that will engage physicians, nurses, pharmacists and social workers to provide optimal care and support that will help women with MS have better outcomes at every stage of life.

Methods: Female MS patients from both CHOP and HUP will be invited to participate in a single focus group. It is anticipated there will be 4 groups. In an open forum style, the group will be asked ten open-ended questions to identify what services they would want to be available in a comprehensive age-span program.

Results: The data will be analyzed using thematic analysis.

Conclusions: It is anticipated that this study will reveal the needs of these women. The ultimate goal will be to develop an Age-Span Program that will meet the needs of this patient population.

Disclosure: *Dina Jacobs: Biogen, Genentech (consulting fee, contracted research). Celgene, EMD Serono, Sanofi-Genzyme (consulting fee). MedImmune (contracted research). Sona Narula, Vanessa Zimmerman: Nothing to disclose.*

Keywords: Age-Span Women's MS Program , Comprehensive care and MS

(PGM05)

National MS Society Pathways to a Cure an in Person Educational Program for People Affected By MS

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Background: Important strategic goals for the National MS Society are to deliver breakthroughs to a cure and expand resources and reach to all those who are affected by MS. The Society strives to empower people affected by MS to solve everyday challenges by informing them, and connecting them to their communities, and the Society so they can be more powerful than the challenges of MS. The Pathways to a Cure in-person program, conducted in cities across the country, is a key initiative in achieving Society goals. The program presented current research findings and strategies to help people meet the everyday challenges that MS imposes on them.

Objectives: The objectives of the program were to 1) increase participant knowledge on the latest research breakthroughs, 2) increase awareness about wellness strategies and services resources that they can act on now to positively impact their health and quality of life and 3) create connections among participants and those within the MS community.

Methods: During 2019, 101 in-person, 3-hour Pathways to a Cure in-person programs were held throughout the US. The program consisted of didactic presentations on current research and wellness and lifestyle strategies. Presentations were followed by a facilitated Q and A session. Participants were requested to complete a post-program survey to assess the impact of the program.

Results: A total of 3,519 individuals participated in the programs. Of those, 71% identified as living with MS, 72% were women, 77% identified as Caucasian, 15% Black or African American, 6% Hispanic or Latino and 2% Asian. Surveys were completed by 2,216 (63%) participants. Survey results demonstrated that 95% of participants agreed

or strongly agreed that the Society is a source of support where they can find solutions, 91% of participants agreed or strongly agreed that they made connections to information, resources, people or other sources of support, 87% of participants agreed or strongly agreed they had increased confidence and support to cope with the challenges of MS following the event and 87% of participants indicated they planned to take action on information they learned.

Conclusions: The National MS Society Pathways to a Cure in-person program reached a large number of people affected by MS throughout the US. Survey results indicate that the objectives of the program were met. This was a successful method to reach people affected by MS with research breakthroughs and practical strategies to help them live their best lives. A next step that is being explored to extend the reach is offering the program virtually through a streaming platform.

Disclosure: *Nothing to disclose.*

Keywords: Comprehensive care and MS, Management of activities of daily living in MS, Wellness

(PGM06)

How Well Do Junior Neurology Residents Recognize Multiple Sclerosis? Analysis of the "Close the Loop" Clinical Acumen Project

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Background:

Multiple sclerosis (MS) misdiagnosis is an important issue with major potential consequences. Residency training is where future neurologists develop their clinical acumen and diagnostic ability. We describe multiple sclerosis/demyelinating disease cases presented by junior neurology residents.

Objectives: To evaluate initial diagnostic accuracy and identify educational needs to prevent MS misdiagnosis and enhance quality of care.

Methods: From July 2010 to June 2016 all patients independently assessed and presented by on-call junior neurology residents during daily morning report were logged, including case demographics and the initial diagnostic impression. Cases were subsequently revisited to “close the loop” with a final diagnosis. Cases were retrospectively categorized as neurological (subdivided by localization and etiology [e.g. MS/demyelinating, stroke]) or “non-neurological”

(e.g., medical, psychiatric) Accuracy of the initial diagnosis was determined and errors were fully characterized.

Results: Of the total 1301 cases, 4.4% carried a final diagnosis of MS/demyelinating disease (n=57). The majority of these patients were evaluated in the emergency department (80.7%) and most were admitted to the neurology service. Resident accuracy for MS/demyelinating disease cases was slightly higher than the overall case accuracy (66.7% vs. 64.0%, respectively). There were 11 cases of MS/demyelinating disease that were initially mistakenly diagnosed as other neurological conditions, Only one MS case was missed at the neurologic/non-neurologic decision-point, while this type of error represented a large proportion of errors in the entire database (49.1%). Residents were more likely to miss true MS/demyelinating disease in men (6/11; 54.5%). Of the 22 cases incorrectly deemed to be MS/demyelinating, 40.9% of errors (9/22) were at the neurologic/non-neurologic level, including 2 psychiatric and 6 medical cases. Diseases mistaken for MS/demyelinating disease include CNS neoplasm (n=3) and ischemic stroke (n=3).

Conclusions: "Close the Loop" represents an educational initiative to provide feedback to neurology residents for improvement in clinical acumen. Despite the relatively small number of MS cases presenting in the acute hospital setting, resident diagnostic accuracy for MS/demyelinating disease was similar to overall accuracy. Analysis of errors made represent an important opportunity to improve recognition and hopefully enhance quality of inpatient care of MS.

Disclosure: *Emily M. Schorr, Jamie Nichols, Rachel Brandstadter: Nothing to disclose. Stephen Krieger: consulting or advisory work with Biogen, EMD Serono, Genentech, Genzyme, Mallinckrodt, MedDay, Novartis, Teva, and TG Therapeutics (consulting fee). non-promotional speaking with Biogen, EMD Serono, Genentech, and Novartis (speakers bureau).*

Keywords: Imaging and MS, Medical education

(PGM07)

Time to Adult: Transitioning from Pediatric to Adult Healthcare in Demyelinating Disorders

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Background:

Transition to adult healthcare is a challenge in pediatric populations with chronic medical conditions, such as multiple sclerosis. Patients require knowledge and proficiency in managing their health, engaging in wellness behaviors, and understanding health insurance and community resources. We developed a formal transition program to support our adolescent patients. Beginning at age 14, patients diagnosed with multiple sclerosis or related disorders and their parents/caregivers complete a questionnaire during annual clinic visits. Questions relate to their readiness to transition, knowledge of their condition, post high school plans, stress and anxiety levels relative to transition, emotional support, quality of life, sleep, and priorities regarding information they would like on future aspects of care. Based on results, tailored education plans are used to improve patient knowledge and proficiency. Patients are tracked over time relative to their successful transition into adult care settings.

Objectives:

Examine the results from patient- and parent-completed questionnaires at baseline and one year post-baseline. Assess improvement in knowledge, readiness to transition and priorities regarding information they would like on future aspects of care.

Methods:

Exploratory analysis of changes from baseline were analyzed using the Wilcoxon signed-rank test when numeric variables were at least ordinal. Binary variables were analyzed using Fisher's exact test. Multiple testing adjustments were not performed.

Results:

To date, 67 patients were seen for baseline visits and 21 returned for a one-year follow-up visit. For those patients who were seen one year post-baseline, there was an increase in the patient- and parent-reported Readiness scores ($p = 0.02$ and $p = 0.001$, respectively). Additionally, there was a decrease in the parent-reported support rating ($p = 0.004$). Lastly, 33 patients and 18 parents ranked a series of future aspects of their care in which they want information with managing their condition as the most important for the majority of participants, followed by medication knowledge.

Conclusions:

Preparing adolescents to manage their own healthcare is critical, especially when faced with a chronic neurologic illness like multiple sclerosis. We noted an increase in patient and parent readiness for transition in our program across time. Future research will seek to identify factors that impact patient ability to successfully transition to adult healthcare.

Disclosure: *Katherine Chapman: Genentech (speakers bureau). Denise Maddox, Lana Harder, Patricia Plumb, Morgan McCreary: Nothing to disclose. Benjamin Greenberg: Alexion, EMD Serono, Novartis, Roche (consulting fee).*

Keywords: Comprehensive care and MS, Psychological issues and MS, Transition and pediatric healthcare

(PGM08)

Successful Pilot of MS VA-Echo Teleeducation Program for Rural Providers

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Background: Comprehensive care for persons with multiple sclerosis (MS) requires expert interdisciplinary teams. While such care is readily available at MS specialty centers in academic and urban environments, healthcare providers who live in smaller cities and in rural areas often do not have MS specialty expertise, and persons with MS living in these rural areas find it difficult to access appropriate care. Solutions are needed for this gap in care.

The Veterans Affairs (VA) Healthcare System's Extension for Community Healthcare Outcomes (ECHO) allows specialists to share expertise with rural providers, enabling these clinicians to provide care not previously available in their communities and to save Veterans from traveling long distances to access specialty care. Although VA-ECHO offers programs in many specialty areas, it did not yet have an MS program. As nearly 29,000 Veterans in the VA Healthcare System live with MS, such a program is needed.

Objectives: 1) To develop a pilot MS VA-ECHO program introducing the basic concepts of MS care most relevant to rural providers, including those which may be managed locally and which may be managed by or in collaboration with specialty MS providers. 2) To analyze audience evaluation of the ECHO presentation in relation to their educational needs and by provider discipline. 3) To ascertain focus for future program development and content.

Methods: We utilized the traditional ECHO 3-part format: 1) didactic material; 2) case study; 3) audience questions and discussion. The pilot session was 75 min. total, with ~45 min. didactic, ~15 min. case study, and ~10-15 min of question-and-answer and discussion. Presenters were a doctorally prepared nurse practitioner (NP) with MS certification and an MS specialist physiatrist, both with extensive practice in MS specialty centers. Content covered an overview of demographics, neuroimmunology and neuropathology, disease-modifying therapies (DMTs), symptom management, and patient and provider resources with special attention to rural applications. Audience metrics were collected.

Results: The audience total of 119 clinicians included physicians, advanced-practice providers, registered nurses, physical, occupational, and speech therapists, pharmacists and social workers, among other disciplines. 96% of the audience found the material relevant to their practice, 45% indicated their practice would change to incorporate information learned, and 95% would like to hear the presenters again. A local focus group of the target audience found that nurses were strongly interested in MS certification. End-of-quarter regional ECHO all-program evaluations included over 400 requests for more MS material.

Conclusions: This pilot MS VA-ECHO session was highly successful. There is demand for an expanded program and for material on MS nursing certification. Program development is underway for the expanded MS VA-ECHO series.

Disclosure: *Lynda R. Hillman: Celgene (advisory). Jodie K. Haselkorn: Nothing to disclose.*

Keywords: Comprehensive care and MS, TeleHealth

(PGM09)

Current Topics in MS Webinar Series a Professional Education Collaboration between the NMSS, CMSC and the VA MS Centers of Excellence

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Background: MS is a complex disease that requires a highly educated workforce. To help meet the educational needs of MS healthcare professionals, the National MS Society (NMSS), Consortium of MS Centers (CMSC) and the Veteran Health Administration MS Centers of Excellence (VAMSCoE) collaborated to develop a professional educational program to provide evidence-based information on MS diagnosis and management.

Objectives: Participants will 1) have easy access to evidence-based content with relevance to a variety of disciplines involved in MS care, 2) gain improved knowledge about MS and MS management, and 3) consider a change in their practice as a result of the information and resources presented.

Methods: An educational program was developed entitled Current Topics in MS and it consisted of six, 1-hour webinars on topics identified by healthcare providers including MS diagnosis, spasticity in MS, rehabilitation/telerehabilitation, reproductive care, MS in the African

American population and depression. Each webinar consisted of a 50-minute didactic presentation followed by a 10-minute facilitated question and answer session. Participants had the option to attend a live webinar or view a recorded presentation. Both were accredited for CME and CE. Following the live webinars, all registrants were sent a link to the webinar recording, and all participants were provided access to a program evaluation survey and a portal to complete a post-test and claim their free educational credits or a certificate of participation.

Results: As of December 1, 2019, 866 healthcare providers (261 VA) attended the live or recorded webinars and 629 (73%) claimed continuing education credit or certificates. Survey results indicated 95% of respondents agreed or strongly agreed that the content was relevant to their current practice, 83% agreed or strongly agreed that participation improved knowledge, and 94% agreed or strongly agreed that participation encouraged them to consider a change to their practice.

Conclusions: The Current Topics in MS webinar series is an important collaborative effort between the NMSS, CMSC and the MSVACoE. The series reached VA and non-VA healthcare providers with free and easily accessible professional education. Survey results indicate that participants found the programs useful and a large percentage planned a change in their practice based upon what they learned. Six new webinars are planned for 2020.

Disclosure: *Nothing to disclose.*

Keywords: Comprehensive care and MS, Diagnosis , Psychological issues and MS

(PGM10)

MS Nurse Fellowship Pilot: A Six Month Immersion

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Background: The current shortage of Registered Nurses (RNs) is expected to intensify as Baby Boomers age and retire from nursing. The retirement wave of these nurses will create a drain on clinical expertise which is critical to quality patient care, especially in MS. It is more difficult to quantify the loss of knowledge and understand its impact than it is to measure projected workforce demands due to retirement. Although nursing schools try to admit more students, they focus on preparing generalist nurses in acute care settings. This has resulted in unpreparedness of the nurse graduate for an independent role focusing on outpatient specialty practices such as MS. New RNs who enter MS practice will need much mentoring to learn to care for patients. This knowledge gap was identified by the International Organization of Multiple Sclerosis Nurses in collaboration with the School of Nursing at the State University at Stony Brook.

Objectives: A pilot program was developed to train a Registered Nurse enrolled in an RN to Bachelors (RNBS) degree nursing program. The student will complete a six-month clinical fellowship in the care of MS patients. RNs in the RNBS program were invited to apply by completing the application, submitting a one-page essay describing their interest and experience in MS, and a reference from a professor. The call for applications described the plan for training and the six-month clinical experience in a mentored environment.

Methods: One (1) student was selected to begin the fellowship in Fall 2019. Knowledge of MS was determined by questionnaires and the student had strong knowledge of nursing but little of MS nursing. The student was then provided with a plan for training and a 6 month clinical experience in a mentored environment.

Results: For the first 3 months, the student was precepted by a certified MS nurse practitioner and MS neurologists. A mid-fellowship student evaluation was developed which showed progress in both knowledge and skills in MS. During the second 3 months, the student will work with neuro-radiology, neuro-ophthalmology, neuro-urology, neuro-psychology and the outpatient department social worker.

Conclusions:

At the completion of the program, both the student and preceptors will complete evaluations documenting outcomes of this unique pilot project. It is anticipated that this program will generate similar training programs nationally and internationally.

Support: This pilot project was funded by the International Organization of MS Nurses supported by an educational grant from EMD Serono.

Disclosure: *Patricia Melville: EMD Serono (speakers bureau). Marijean Buhse, June Halper: Nothing to disclose.*

Keywords: Nursing Fellowship, Nursing management in MS

(PGM11)

Collaborative Working between Multiple Sclerosis (MS) Nurses and a Pharmaceutical Company: An Educational Project from the Consortium of Multple Sclerosis Centres (CMSC) Conference, Seattle 2019

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Background:

Work collaboratively with key MS Nurses from the United Kingdom and a pharmaceutical company in an educational project that has been shared with the wider UK MS community.

Objectives:

To share recent experience and reflections at the Consortium of Multiple Sclerosis Centres (CMSC) conference as part of a small focus group of United Kingdom (UK) Multiple Sclerosis (MS) Nurses.

Methods:

Five nurses were supported by Roche to participate as a focus group of delegation to CMSC. The group met prior to the conference with the Roche team and a medical writer. The agenda was reviewed and relevant topics/ sessions were chosen and divided between the delegates, dependent on skill set and areas of interest and experience. The sessions chosen were areas of interest not only from the delegate's point of view, but also what would benefit the wider MS community in the UK.

Results:

The delegates attended the sessions (including the poster session) and fed back key learning messages attained to the medical writer using an agreed designed template. The delegates also had the opportunity to share with each other current practices, challenges and share experiences from areas of practice. This provided not only clinical supervision, but also reflection of own practice.

From the feedback of the delegates, the medical writer produced a slide deck. The slide deck was given to the delegates to keep and to present to local members of their team and to the wider region. In addition, this slide deck is the intellectual property of the five delegates and will also be available via the United Kingdom Multiple Sclerosis Specialist Nurse's Association (UKMSSNA) slide deck library.

Conclusions:

This innovative project not only benefits the delegates, it also disseminates all learning and knowledge acquired to the wider MS communities. This way of working also provides greater transparency between the relationship of the sponsoring pharmaceutical companies and the delegates.

The delegates unanimously recommend this strategy of working during conferences and perhaps should be adapted by the rest of the pharmaceutical industry and health care professionals.

Disclosure: *Mavis G. Ayer: Biogen, Roche (sponsored delegate). Celgene, Merck, Novartis, Sanofi (consulting fee). Teva (sponsored education). Karen Vernon, Carmel Wilkinson: Biogen, Merck, Novartis, Roche, Sanofi, Teva (consulting fee). Lynda Kearney: Biogen, Novartis, Roche, Sanofi (consulting fee). Brenda Hamill: Biogen, Novartis (sponsored delegate). Roche (consulting fee).*

Keywords: Sharing Best Practice

Psychosocial Factors

(PSF01)

Differences in Depressive Symptomology between Females and Males with Relapsing-Remitting Multiple Sclerosis

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Background: Up to 50% of individuals with Multiple Sclerosis (MS) experience depression, which greatly impacts quality of life (Feinstein et al., 2014). Previous studies on depression in the general population have found that prevalence and reported symptoms differ as a function of gender, with higher rates in women (Salk et al., 2017). However, there are few studies on gender differences in symptoms of depression for people with MS, and the limited findings to date have been mixed (Patten et al., 2003; Théaudin et al., 2016).

Objectives: The current study aimed to investigate whether there are differences between females and males with Relapsing-Remitting MS (RRMS) in overall depression scores as well as the types of depressive symptoms reported (somatic or cognitive).

Methods: Demographic and Beck Depression Inventory, 2nd edition (BDI-2) raw scores for females and males with RRMS were downloaded with permission from the Multiple Sclerosis Outcome Assessments Consortium database (LaRocca et al., 2018). In addition to BDI-2 Total Scores, BDI-2 Somatic and Cognitive scores were also calculated for each participant (Beck et al., 1996; Vanheule et al., 2008). All statistical analyses were performed using RStudio. Data were first visually inspected using QQ-plots, followed by the Shapiro-Wilk Test of Normality, which indicated that the data deviated significantly from a normal distribution ($p < .001$). Thus, non-parametric Wilcoxon rank-sum tests were used to compare BDI-2 Total Scores, BDI-2 Somatic Scores, and BDI-2 Cognitive Scores between females and males with RRMS.

Results: Responses from 354 females with RRMS and 140 males with RRMS were included in the analysis (mean age = 35.8 ± 9.5 years females; 37.4 ± 10.2 years males). Females reported significantly higher levels of overall depression (median = 9) compared to males (median = 7), p = 0.032. Furthermore, females endorsed significantly greater somatic symptoms (median = 7) than males (median = 5), p = 0.026. There were no significant differences in females' reports of cognitive symptoms (median = 2) compared to males' (median = 1), p = 0.12.

Conclusions: Females with RRMS report higher levels of overall depression and somatic depressive symptoms compared to males with RRMS. Future research should focus on individuals with primary and secondary progressive MS to evaluate whether patterns of depressive symptomatology differ between females and males with progressive forms of MS.

Disclosure: *Nothing to disclose.*

Keywords: Depression, Psychological issues and MS

(PSF03)

Metoo MS: Physical, Sexual and Other Forms of Violence Experience in Women with Multiple Sclerosis

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Background: Sexual and physical violence against individuals with disabilities is widespread and linked to negative public health and social outcomes. In the past decade, emotional, physical, and sexual abuse of women with chronic illnesses and physical or cognitive disabilities has become increasingly recognized by public and healthcare providers. Women with disabilities have a higher likelihood of abuse, due to dependency on others, and stigma that surrounds their illness.

Objectives: To explore the real-world prevalence of sexual, physical and other forms of abuse and their correlation with neurologic disability in women with multiple sclerosis (MS).

Methods: Women with MS who saw a neurologist at the Partners MS Center between 7/31/19 and 10/21/19 were invited to participate in the study. They received a standardized anonymous questionnaire querying their previous sexual, physical, verbal and emotional abuse experiences. Demographic information was collected on age, education, employment, and marital status.

Results: 200/830 women (24%) completed the questionnaire. Mean age (SD) was 49 (11.39) years and mean disease duration (SD) was 13 (8.67) years. 129 women (64.5%) were married or with a long-term partner. 134 patients (67%) were employed full or part-time. 186 women self-identified as heterosexual (93%), 8 (4%) were bisexual, and 5(2.5%) were homosexual. 76/200 respondents (38%) reported some form of abuse at any point in time, 11/76 (14.4%) reported abuse over the preceding 12 months; 15 (20%) patients reported physical and/or sexual abuse, 19 (25%) reported verbal abuse and 42 (55%) reported both physical and verbal abuse**.** 36 (47%) patients received professional help in dealing with the aftermath of the experience. 2/76 (3%) patients identified themselves and asked to be contacted by the healthcare team. Married women or those in domestic partnership were more likely to report any form of abuse than single patients ($p<0.0207$). Any level of current neurologic disability was associated with a higher likelihood of ever experiencing verbal abuse ($p = 0.021$). There was no association between physical ($p=0.0734$) or verbal abuse ($p=0.363$) and neurological disability using the Chi-square test. There was no association between these variables when adjusting for age and education based on a logistic regression model ($p=0.860$).

Conclusions: 38% of respondents acknowledged some form of abuse in their past. This proportion is higher than that reported in the general female population (29%). Less than 50% of affected women ever sought professional help in dealing with the trauma. Intimate partner violence in married or partnered women with MS may be more prevalent than previously recognized. Lower than expected anonymous questionnaire response rates suggest persistent patient discomfort in addressing this difficult matter. This study will continue recruiting subjects to increase the power of our observations.

Disclosure: *Jeta Pol-Patil, Maria Claudia Manieri, Tatenda Mahlanza, Elizabeth Misasi, Laura T. Safar: Nothing to disclose. Bonnie Ilene Glanz: Merck Serono, Verily Life Sciences (grant support). Maria K. Houtchens: Biogen, Celgene, Genzyme Sanofi, Mallincrodt, Serono (consulting fee).*

Keywords: Physical and sexual violence, Psychological issues and MS

(PSF04)

Predictors for Self-Efficacy for People Living with MS

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Background:

The Multiple Sclerosis Achievement Center (MSAC) is a community wellness rehabilitation program for individuals with progressed MS. This site provides services in order to enhance quality of life and provide a sense of community for members. Services provided at this site include occupational therapy, physical therapy, social activities, and mental health groups.

There is little evidence that focuses on predictors for self-efficacy in individuals with progressed MS in the literature. This research studied the effect of participation at MSAC in relation to feelings of self-efficacy from the perspective of individuals with MS by reviewing and analyzing data that is regularly collected on MSAC participants.

Objectives:

The objectives of this study were to:

- Analyze data on pain, fatigue, outside activities, and participation in program activities for members of the MSAC
- Analyze data on self-efficacy scale for participants of MSAC

Methods:

This study looked at data collected as part of MSAC. This data included information from forms about levels of fatigue, pain level, medical concerns, outside activities, and social isolation that are collected each week from members. The Multiple Sclerosis Self-Efficacy Scale (MSES), which consists of person-rated perception of ability to overcome challenges one is faced with, was also collected and analyzed. Sample size included 50 individuals (36 women and 14 men) that are members of the MSAC. This was an observational, cross-sectional design and correlational analysis investigated the relationships between pain, fatigue, activity outside of the program, and participation in program activities and feelings of increased self-efficacy.

Results:

The results indicate no significant correlations between the total MSSE score and individual participant factors. However, results suggest that doing-based questions have a stronger relationship with self-efficacy (β=.505; p=<0.001) than feeling-based questions (.411β; p=<0.001). When completing a correlational analysis of the total self-efficacy scores, doing-based questions also have a higher correlation (β=.640) than feeling-based questions (β=.577) in comparison to total MSSE scores.

Conclusions:

The results indicate that both the ability to perform activities of daily living and feelings related to MS have an impact on levels of self-efficacy in this population. However, it suggests that the ability to perform tasks and activities of daily living had the most significant impact on participants self-efficacy scores.

Disclosure: *Nothing to disclose.*

Keywords: Comprehensive care and MS, Psychological issues and MS, Wellness

(PSF05)

The Association between Health Literacy, Health Outcomes, and Medication Adherence in Patients with Multiple Sclerosis

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Background: Multiple sclerosis (MS) is an immune-mediated disorder characterized by demyelination of nerve cells within the brain and spinal cord over a period of time. Historically, MS was considered an untreatable disease; however, there are currently over a dozen disease modifying therapies approved by the FDA. A potential barrier to receiving a diagnosis and treatment of MS is health literacy, which is described as the degree to which individuals have the capacity to obtain, access, and understand basic health information and services needed to make appropriate decisions.

Objectives: The purpose of this study is to investigate the relationships between health literacy, health outcomes, and medication adherence in patients with multiple sclerosis.

Methods: This study was a single-site, prospective study done at the multiple sclerosis center at the University of Rochester Medical Center. Health literacy was measured using the Short Test of Functional Health Literacy in Adults.

Results: Of the 179 subjects included in the analysis, 178 had adequate health literacy, 1 had marginal health literacy, and 0 had inadequate health literacy.

Conclusions: The relationship between health literacy, health outcomes, and medication adherence cannot be determined in this sample given the lack of variability in health literacy.

Disclosure: *Nothing to disclose.*

Keywords: Health literacy

(PSF06)

It Takes a Village: The Veterans Health Administration (VHA) MS Centers of Excellence and National Multiple Sclerosis Society Partnership for Facilitating Communication, Collaboration and Coordination of Services for Veterans with MS

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Background: Currently, there are 22 million Veterans. Only 8 million of these Veterans are enrolled with the Veterans Health Administration (VHA). 70% of these Veterans receive additional health, support services, and care coordination from private sector providers outside of the VHA. The VA MS Centers of Excellence (MSCOE) supports comprehensive specialty care teams across the VHA who evaluate, treat, and provide ongoing care management to over 24, 000 Veterans living with MS in the USA. MS Clinics across the VHA system provide comprehensive MS care through MS Specialists including rehabilitation services, neurology, nursing, social work, and neuropsychology. In addition, VHA system provides home health aide services and caregiver support to assist Veterans with MS remain independent in their community.

Objectives: Through a collaborative partnership, VHA MSCOE and The National MS Society (NMSS) developed a formal process for mutual communication and coordination of resources for Veterans w/MS: 1) VA MSCOE Social Workers provide VHA 101 educational webinars to MS Navigators that address unique needs of Veterans with MS and their families, providers, and care partners. 2) To establish a process of case consultations that involve Veterans who contact the MS Navigators with complex resource, support, or benefit needs. 3) Identify Veterans who could benefit from MS Navigator Program and send referrals from VHA.

Methods: 1) The MSCOE Social Work Staff developed and provided training presentations (VHA 101) to educate MS Navigators about Veteran culture, VHA eligibility, enrollment, programs and care navigation.

2) Point of contacts were established for both the MSCOE and NMSS for discussing complex Veteran cases.

3) Case consultations between MS Navigators and MSCOE Social Work staff proceeded routinely.

Results: Over 80 MS Navigators participated in VHA 101 webinars provided by VHA MSCOE Social Work staff. Case consultations between MS Navigators and VHA MSCOE Social Work staff were successfully resolved. Types of referrals between VHA and the MS Navigator Program were identified and increased including Veterans benefits, VA MS specialty care services, VA and National MS Society funding. For example, VA Puget Sound referred 22 Veterans to the MS Navigator program for MS educational material, support groups; and financial assistance for Veterans for bills, gym memberships, driver's license, adaptive driving equipment not covered by VA, scooter lift installed, and bed bug eradication.

Conclusions: Preliminary outcomes from educational trainings, individual case consultations, and the referral process have been effective between VHA/MSCOE and NMSS's MS Navigator Program. Education on how each organization operates and provides care and services for Veterans has enhanced the level of information sharing and referrals, thus improving care. Additional presentations and trainings are being planned for both organizations.

Disclosure: *Nothing to disclose.*

Keywords: Comprehensive care and MS, MS and the caregiver/family, Psychological issues and MS

(PSF07)

Discussing Multiple Sclerosis (MS) Progression with Patients: Experiences of UK Healthcare Professionals from the Spectrum Project

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Background: Receiving a diagnosis of secondary progressive multiple sclerosis (SPMS) can have a significant psychological impact on patients. Identifying how and when to initiate discussions about MS progression may be challenging for healthcare professionals (HCPs).

Objectives: To understand how HCPs in the UK discuss the progression from relapsing-remitting multiple sclerosis (RRMS) to SPMS with patients.

Methods: Interviews were conducted in 2019 with 59 HCPs from geographically-dispersed UK MS centres (MS neurologist, n=41; MS specialist nurse, n=15; other HCP, n=3), using a structured questionnaire. Topics covered included current practices for defining, diagnosing and managing SPMS, and discussing SPMS with patients. This analysis focuses on discussing SPMS with patients. n<59 indicates missing responses.

Results: Progression from RRMS to SPMS is most commonly discussed with patients at the following time points (not mutually exclusive): when the SPMS diagnosis is confirmed (n=56/58, 97%), when a patient asks about SPMS after researching their condition (n=56/58, 97%) or when SPMS is first suspected (n=45/58, 78%). Only 20/58 HCPs (34%) discuss SPMS at initial RRMS diagnosis and 28/58 (48%) during the RRMS disease course. Most HCPs (n=43/57, 75%) reported that a neurologist is usually the first person to discuss progression with the patient. The most common terms used by HCPs when discussing SPMS with patients were ‘progression or progressive’ (n=45/59, 76%), followed by ‘transition’ (n=19/59, 32%), ‘worsening’ (n=16/59, 27%) and ‘disability’ (n=9/59, 15%). However, a number of HCPs

reported that they would specifically avoid using the same terms ('disability' [n=13/59, 22%], 'progression or progressive' [n=10/59, 17%], 'worsening' [n=8/59, 14%], 'transition' [n=4/59, 7%]). The median estimated time between first suspecting and diagnosing SPMS was 12.0 months (IQR 12.0–24.0, *n*=45). The most common explanations for reluctance to diagnose SPMS were *concerns over withdrawing treatment* (*n*=49/59, 83%) and *psychological impact on patients* (*n*=39/59, 66%).

Conclusions: There is substantial variation in the UK in both how and when HCPs discuss the transition from RRMS to SPMS with patients. Discussions may be delayed until SPMS is suspected or even confirmed, which can take a year or more. Further training and support for HCPs may be needed in order to facilitate discussions with patients about MS progression and provide them with appropriate support during the transition phase.

Disclosure: *Carmel Wilkinson: Novartis, MedDay (contracted research). Novartis (consulting fee). Katherine Rhys: Novartis (salary).*

Keywords: Progressive MS, Psychological issues and MS

(PSF08)

Development and Implementation of a Patient Education and Cognitive Wellness Program for Veterans with Multiple Sclerosis

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Background: Multiple sclerosis (MS) is a complex chronic disease that affects neurologic, psychiatric, and cognitive functions. Symptoms in these domains can adversely impact functioning and quality of life. Recent epidemiologic studies document higher MS incidence rates among military personnel compared to the general population. To date, no comprehensive group psychotherapeutic wellness intervention addressing the various factors impacting Veterans with MS has been disseminated to our knowledge.

Objectives: 1) To describe the development of a cognitive rehabilitation and psychotherapeutic wellness group intervention for Veterans with MS; 2) To improve cognitive functioning in daily life and facilitate implementation of strategies for coping with cognitive, emotional, physical, and social challenges posed by MS.

Methods: Content for an introductory 7-week group entitled MS Intervention and Development of Skills (MINDS) and an advanced, part two, 7-week group entitled Master MINDS was

adapted from various existing cognitive rehabilitation programs and tailored to Veterans with MS. Sessions included psychoeducation regarding MS symptoms, compensatory strategies to address the cognitive domains often impacted by MS (attention, memory, processing speed, executive functioning), methods for enhancing positive health behaviors, including strategies to cope with fatigue, depression, psychosocial stress, and social role changes, and discussion of relevant VA and community resources. Guest speakers from other disciplines in MS care were invited to facilitate two didactic and Q&A sessions. Importantly, Veteran feedback was sought throughout each session and used to develop two new modules related to parenting with MS (Caring MINDS) and specific issues related to men with MS (Mr. MINDS).

Results: Six Veterans participated in the groups and completed self-report questionnaires assessing mood (PHQ-9) and subjective cognitive impairment (MSNQ) pre- and post-intervention. Examination of scores revealed that most reported stable or improved mood while half reported stable or lower risk of depression and/or cognitive impairment post MINDS. Post Master MINDS, most reported stable or improved mood and stable or lower risk of depression and/or cognitive impairment (one participant missing).

Conclusions: Group intervention for Veterans with MS is a viable treatment modality and content tailored to this population is subjectively useful in improving mood and increasing awareness of the cognitive, emotional, physical, and social challenges associated with MS. Therapeutic factors such as the instillation of hope, social support, validation of concerns, and interpersonal learning were identified by group members as key elements of the intervention. Finally, patient-centered feedback was critical in developing tailored treatment plans and additional modules.

Disclosure: *Nothing to disclose.*

Keywords: cognitive rehabilitation, Psychological issues and MS

(PSF09)

The Effects of Customized Psychoeducation-Based Neurocounseling Interventions on the Coping Flexibility of African American Women with Multiple Sclerosis

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Background: The importance of adaptive (i.e., effective) coping strategies among people with multiple sclerosis (PwMS) has been well documented in the literature. However, a gap in the body of knowledge related to African American women living with this chronic disease still exists. Historically, their coping behaviors, emotional support needs, and mental health have not been a focus in the MS literature. As a result, the challenges, needs, and perspectives of Black

women living with MS is limited and deserves more scholarly attention and a great need exists to help this underserved and under researched population with their coping efforts. This study examined the effectiveness of a Brain-Based Education and Wellness (BE WELL) intervention on the coping flexibility of African American women with Multiple Sclerosis (MS).

Objectives: 1) To learn about the conceptual framework for the Brain-Based Education and Wellness (BE WELL) program 2) To examine the effects of customized psychoeducation-based neurocounseling interventions on the coping flexibility of African American women with MS 3) To assess participants' social validity ratings of the BE WELL intervention program.

Methods: An N-of-1/ A-B-A single-case research design (SCRD) was used for this 12-week intervention study. Data were examined using both visual and statistical analysis. This involved using descriptive statistics including measures of central tendency and variability, autocorrelations, and regression analysis to look for trends. The G index was used to calculate effect sizes and the non-parametric test Conservative Dual-Criteria (CDC) was used as a robust statistical analysis tool to compare the phases of each coping measure.

Results: The participants were four African American women with MS ages 34 to 60. For three participants, Aggie, Chelsea, and Tonya, there were large to medium effect sizes (ES=.50 to ES=1) for one or more coping measures in the baseline to withdrawal phase. For Participant 2, Yvonne, there was only a medium effect size for evaluation coping (ES = .50) from treatment to withdrawal phase. Participants' social validity ratings from the ATT ranged from 87-98 indicating that each participant found the intervention to be valuable.

Conclusions: The customized BE WELL intervention seemed to have positive effects for each of the participants' coping flexibility. Participant 2, Yvonne, was the exception as only slight effects were observed. For three participants, the most profound effects occurred in evaluation coping. Results from the ATT validated the findings from the visual and quantitative analysis as all participants' ratings revealed that each participant experienced positive treatment effects from the BE WELL program.

Disclosure: *Nothing to disclose.*

Keywords: Management of activities of daily living in MS, Psychological issues and MS

(PSF10)

The Conformity of Masculine Norms and the Effects on Coping, Health Behaviors, and Quality of Life in Men with Multiple Sclerosis

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Background:

The aim of the project is to explore how the conformity of masculine norms effects coping, health behaviors, and quality of life in men with multiple sclerosis. Despite some documented concerns of men with MS (e.g. prognosis, quality of life, targeted interventions) (Upton & Taylor, 2015), the specific conformity of socialized masculinity and gender norms affecting men with MS has not received attention in the academic literature. According to Levant and Wimer (2014) masculinity conformity is complex in nature due to finding some gender performance to be protective and others to be detrimental when it comes to men's health. It is unknown how masculinity conformity affects men with MS, specifically in terms of its association with coping, health behaviors, and quality of life. This study aims to explore these factors in order to evaluate the experiences of men with MS. Such information will fill a void in the literature and inform future interventions to better serve men with MS.

Objectives: Examine and describe the association between masculinity conformity, coping, health behaviors, and quality of life in a representative sample of men with MS.

1.Hypothesis: Higher scores on the masculinity inventory will produce lower/worse scores on health-related quality of life.

Subaim: Investigate the differential effect of coping and masculinity conformity on quality of life.

2. Hypothesis: Men with higher scores on the masculinity inventory will have less/worse coping which will negatively impact quality of life more than for men with lower scores on the masculinity inventory (independent of coping ability).

3. Hypothesis: Higher scores on the masculinity inventory will produce lower/worse scores on health-related quality of life.

Subaim: Investigate the differential effect of coping and masculinity conformity on health behaviors.

Methods: Participants in this study will include adult (18+ years) men with MS who are established patients at the Mellen Center (Cleveland Clinic). Demographic Information (age, race, marital status, household income, and education status) and clinical characteristics (years since MS diagnosis, Patient Determined Disease Steps (PDDS)), and five patient-reported outcomes will be collected:

1. The Conformity of Masculinity Inventory-46 which is a short version of the CMNI (Mahalik et al., 2003) will be used to assess the conformity to nine masculine norms.
2. Health-related quality of life will be assessed with the PROMIS Global Health (Hays 2009).

3. The Ways of Coping Questionnaire (WCQ) (Lazarus and Folkman, 1985) will be used to measure coping.
4. Health behaviors will be measured using the Health Behaviors Inventory-20 (HBI-20).
5. Disease impact will be evaluated using MS Performance Scales.

Results: Research initiated January 2020, Results expected in Spring of 2020

Conclusions: Research initiated January 2020, Results expected in Spring of 2020

Disclosure: *Nothing to disclose.*

Keywords: Gender Issues, MS and the caregiver/family, Psychological issues and MS

(PSF11)

Understanding the Lived Experience of Health through the Exploration of Well-Being of Women with Multiple Sclerosis: Preliminary Findings

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Background: There are approximately 100,000 Canadians with MS, a condition which is three times more likely to impact women compared to men. Existing evidence proposes that women may experience disability, social determinants of health and their overall health differently than men. Therefore, current evidence may benefit from researchers exploring gender as a category for investigation of phenomena related to health. The World Health Organization [WHO] defines health as physical, mental and social well-being and is underpinning the exploration of health in women with MS for this study. Limited evidence is presently available as to how women in Canada living with MS experience their health through physical, social and mental well-being.

Objectives: The purpose of this hermeneutic phenomenological study is to understand the essence of the lived experiences of women affect by MS living in Southwestern Ontario Canada for health in the context of physical, social and mental well-being.

Methods: van Manen's hermeneutic phenomenological approach was utilized to explore the experience of health through the context of physical, social and mental well-being for participants. Participants included 20 women affected by MS living in Southwestern Ontario, Canada who were interviewed using semi-structed interview guides that were audio-recorded, transcribed verbatim and analyzed using van Manen's interpretive phenomenological approach which consisted of extracting significant statements and themes for the investigated phenomena.

Results: Preliminary results from this study will be presented at this conference as to how women experience health through their well-being and will be discussed in an oral presentation.

Conclusions: A preliminary review of the findings of health through the context of social well-being, such as barriers or factors that promote the overall health and well-being for women affected by MS will be presented. Further exploration as to how social well-being and various social determinants of health impact health through the context of physical, social and mental well-being is needed to further extrapolate these preliminary findings of the study.

Disclosure: *Nothing to disclose.*

Keywords: Comprehensive care and MS, Nursing management in MS, Self care and MS

Quality of Life and Outcomes

(QOL01)

Alemtuzumab Effects on Urogenital Function: Results Pooled From the CARE-MS 9-Year FAMS Quality-of-Life Survey

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Background: Nearly all MS patients (pts) experience urogenital dysfunction within 10 years (y), resulting in significant impacts on quality of life (QoL). Few studies have measured the effects of disease-modifying therapies (DMTs) on this aspect of disability. In the CARE-MS trials (NCT00530348, NCT00548405), alemtuzumab showed greater improvements in clinical, MRI, and QoL outcomes versus SC IFNB-1a over 2 y in RRMS pts, and efficacy was maintained in 2 consecutive extension studies (NCT00930553, NCT02255656).

Objectives: Determine the effect of alemtuzumab treatment on urogenital function over 9 y in pooled CARE-MS pts.

Methods: Pts received either SC IFNB-1a 44 μg 3x/week or 2 alemtuzumab courses (12 mg/day; baseline [BL]: 5 consecutive days; 12 months later: 3 consecutive days) in the core studies, with additional alemtuzumab as needed in the extensions (3 consecutive days, ≥12 months after the most recent course) or other DMTs. Items on the Functional Assessment of MS (FAMS)

questionnaire pertaining to urination frequency, bladder control, and sexual function (for pts who had been sexually active within 1 y) were assessed. Pts rated their perceptions on a 0−4-point scale and considered the previous 7 days in their responses.

Results: In the alemtuzumab group (n=798), mean urination frequency rating was 1.04 at BL, improved to 0.93 at Y2 (*P*=0.002 vs BL), and was 0.96 at Y9 (*P*=0.94); 73% of responses at Y9 rated at 0 or 1 (indicating normal frequency). Mean urination frequency rating in SC IFNB-1a pts (n=386) was 1.11 at BL and 1.04 at Y2 (*P*=0.01 vs alemtuzumab at Y2). Mean urine control rating in alemtuzumab pts was 0.91 at BL, 0.86 at Y2 (*P*=0.28 vs BL), and 0.93 at Y9 (*P*=0.035); 76% of responses at Y9 rated at 0 or 1 (indicating good control). SC IFNB-1a pts rated urine control as 0.88 at BL and 0.84 at Y2. FAMS urine control ratings and EDSS bowel/bladder functional system (FS) scores in the alemtuzumab group were highly correlated (Spearman coefficient at Y2, 0.5695; *P*<0.0001). Mean sexual satisfaction rating for alemtuzumab pts was 2.50 at BL, 2.57 at Y2 (*P*=0.20 vs BL), and 2.62 at Y9 (*P*=0.56); >60% of responses at Y9 rated at 3 or 4 (indicating high satisfaction). Mean sexual satisfaction rating in SC IFNB-1a pts was 2.44 at BL and 2.45 at Y2 (*P*=0.047 vs alemtuzumab at Y2).

Conclusions: Alemtuzumab-treated pts' perception of urine frequency and bladder control, and satisfaction with sexual function were stable over 9 y after initiating alemtuzumab.

STUDY SUPPORT: Sanofi and Bayer HealthCare Pharmaceuticals.

Disclosure: *Aaron Boster: Biogen, Mallinckrodt, Medtronic, Novartis, Sanofi Genzyme, Teva (consulting fees and/or fees for non-cme services). Sanofi (advisor for participating on the managed care review panel). Rafael Arroyo: Almirall, Bayer, Biogen, Merck, Novartis, Roche, Sanofi, Teva (speaking fees from and advisory board participant). Antonio Bertolotto: Biogen (consulting fee, lecture fees). Genzyme (consulting fee). Merck, Novartis, Roche, Sanofi, Teva (lecture fees). Samuel F. Hunter: AbbVie, Acorda, Actelion, ADAMAS, Alkermes, Avanir, Bayer HealthCare, Biogen Idec, Genzyme, Novartis, Osmotica, Questcor, Roche, Sanofi, Synthon, Teva (consulting agreements, speaker honoraria, and grant/research support). Carolina Ionete: Biogen, Roche (contracted research). Sanofi (compensation for advisory board participation, contracted research). Bart Van Wijmeersch: Actelion, Bayer-Schering, Biogen, Merck Serono, Novartis, Roche, Sanofi, Teva (research and travel grants, honoraria for ms-expert advice, and speaker fees). Ericka M. Bueno, Nadia Daizadeh, Elizabeth M. Poole: Sanofi (salary). Bhupendra O. Khatri: Acorda, Celgene, Serono, Teva (consulting/honorarium (consulting work, and speaker programs)). Alexion, Biogen, Genentech, Novartis, Sanofi (consulting/honorarium (consulting work, and speaker programs), contracted research). Ra Pharmaceuticals (contracted research).*

Keywords: Disease-modifying treatments in MS, Management of activities of daily living in MS

(QOL02)

The Impact of Relapses on Quality of Life in Patients with Neuromyelitis Optica Spectrum Disorder: Data from the Phase 3 Prevent Study

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Background: Data are lacking on the impact of relapses on patients with neuromyelitis optica spectrum disorder (NMOSD). PREVENT (NCT01892345) was a randomized, double-blind study of eculizumab in patients with aquaporin-4 immunoglobulin-G positive NMOSD, which showed a 94% reduction in the risk of adjudicated relapse versus placebo; it also included survey assessments of health-related quality of life.

Objectives: To evaluate the effect of relapse on quality of life in patients with NMOSD, using data from the phase 3 PREVENT study.

Methods: Patients' health-related quality of life was assessed using the EuroQol 5-Dimensions questionnaire (EQ-5D) and the Medical Outcomes Study Short-Form (36-item) Health Survey (SF-36), with higher values in both indicating better health-related quality of life. In the current *post hoc* analysis, data from the eculizumab and placebo groups were pooled and the last recorded EQ-5D and SF-36 scores before an adjudicated relapse were compared (at relapse level) with post-relapse scores (recorded ≥ 30 days after relapse) using a paired *t* test.

Results: In the absence of relapse, EQ-5D and SF-36 scores were stable over time, as expected. Mean scores before (n=24) and after (n=22) relapse were: EQ-5D index (possible range 0–1): 0.656 and 0.595, respectively (pre–post difference, –0.067; $p = 0.012$); EQ-5D visual analog scale score (possible range 0–100): 60.458 and 56.500, respectively (pre–post difference, –4.227; $p = 0.226$); SF-36 physical component summary score (possible range 0–100): 38.487 and 36.431, respectively (pre–post difference, –2.602; $p = 0.049$); and SF-36 mental component summary score (possible range 0–100): 45.300 and 41.774, respectively (pre–post difference, –3.164; $p = 0.041$). There were significant differences between pre- and post-relapse scores in the SF-36 domains of bodily pain ($p = 0.027$), physical functioning ($p = 0.007$), role-emotional ($p = 0.021$) and vitality ($p = 0.025$).

Conclusions: This analysis suggests that relapses in patients with NMOSD are associated with a significant reduction in certain aspects of quality of life beyond the immediate relapse period.

Disclosure: *Achim Berthele: Alexion Pharmaceuticals (consulting fee, contracted research, fees for non-cme/ce services received directly from commercial interest or its agent, speakers bureau). Michael Levy: Alexion Pharmaceuticals (consulting fee, contracted research, fees for non-cme/ce services received directly from commercial interest or its agent). Genentech, Quest Diagnostics, Viela Bio (consulting fee, fees for non-cme/ce services received directly from commercial interest or its agent). Karissa Johnston, Meagan Harwood: Nothing to disclose. Adrian Kielhorn, Minying Royston: Alexion Pharmaceuticals (salary). Guido Sabatella: Alexion Pharmaceuticals (ownership interest, salary). Jacqueline Palace: Biogen, Chugai (contracted research). LEK, Viela*

Bio, Guidepoint (consulting fee). Merck Serono (meeting/lecture/workshop participation). Novartis, Roche, Argenx (speakers bureau). UCB, Viela Bio, Roche (conference/lecture participation).

Keywords: Quality of life in NMOSD

(QOL04)

Understand Common MS Symptoms Experienced Among MS Patients Participating in an Online MS Community

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Background: People with multiple sclerosis often seek perspectives and support from each other by connecting on patient social networks. These organic interactions provide unfiltered, rich insight into the day-to-day challenges and needs of patients, including both the emotional and physical issues they face. Directly understanding the holistic impact of MS on patients is crucial to treating patients, including improving doctor-patient interactions and enabling patients to better manage their MS.

Objectives: Leverage the largest MS patient social network in the world to understand the most prevalent symptoms of MS patients as they reach out to one another for information and support.

Methods: Research conducted on de-identified organic discussions within MyMSTeam.com, a social network >127,000 PwMS in the US. Using Natural Language Processing (NLP), 178,884 verbatim discussions from April -September 2019 were analyzed. Key themes were identified and utilized to determine common symptoms and sentiment.

Results: 40% of the discussions were about symptoms, which were highly negative (60%). Most prevalent discussion was pain (35% of symptom discussions), especially leg pain. While members turned to medicines such as Gabapentin, they also sought out less traditional approaches like CBD in search of pain relief. Other common symptoms discussed included mobility issues and fatigue, but also the emotional impact of MS (depression and anxiety). While slowing MS progression is being addressed by their HCP, MS symptoms were often not being treated, especially depression and anxiety.

Conclusions: Understanding the physical and emotional symptoms that accompany MS but that are not always shared between patients and their doctors can help HCPs provide a more holistic approach to treating MS patients. This includes helping MS patients understand what symptoms they are likely to experience and how they can mitigate them.

Disclosure: *Beth Schneider: MyHealthTeams (contracted research).*

Keywords: Comprehensive care and MS, Management of activities of daily living in MS, Psychological issues and MS

(QOL05)

Uncovering the Needs and Gaps in Care Among MS Patients Participating in an Online MS Community

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Background: People with multiple sclerosis (MS) often seek perspectives and support from each other by connecting on patient social networks. These organic interactions provide unfiltered, rich insight into the day-to-day challenges and needs of patients that are not always raised with HCPs. They also uncover attitudes towards and perceptions of disease modifying therapies that sometimes are a surprise to HCPs. Directly understanding the key challenges, concerns and habits of people with MS (PwMS) can elevate doctor-patient interactions and enable patients to better manage their MS.

Objectives: Leverage MS social network to obtain key insights, and understand key issues and challenges of MS patients that could be helpful to HCPs treating people with MS.

Methods: Research conducted with de-identified organic verbatims within MyMSTeam.com, a social network >127,000 PwMS in the US. Using Natural Language Processing (NLP), 178,884 verbatim discussions from April -September 2019 were analyzed. Key themes were identified and utilized to determine positive or negative sentiments.

Results: 40% of the discussions were about symptoms with pain being the most discussed,15% about the doctor-patient relationship, 10% Disease Modifying Treatments (DMTs) and 6% on symptomatic medications. Discussions revealed that depression and anxiety that accompany MS are often under-treated and that pain can be relentless, especially leg-pain. Approximately 18% of the conversations focused on supporting one another. Social conversations were extremely positive and well received (“I feel less isolated since joining this team.”), while conversations focused on living with MS were generally negative especially the profound impact of MS on quality of life.

Conclusions: The organic interactions among patients living with MS provided deeper understanding of symptoms, challenges, attitudes to treatment and steps taken to mitigate MS in ways that are not often shared between patients and doctors. Understanding the needs of these patients provides significant opportunities for HCPs to better support and educate their patients. This includes setting the right expectations, addressing the impact of MS holistically, including pain, depression and other symptoms, and providing tools and education materials to

help stay the course. The research also suggests that encouraging MS patients to connect with one another can help alleviate some of the isolation and depression.

Disclosure: *MyHealthTeams (contracted research).*

Keywords: Comprehensive care and MS, Management of activities of daily living in MS, Psychological issues and MS

(QOL06)

System-Level Variation in All-Cause Hospitalizations in MS: Year 1 Results of the Multiple Sclerosis Continuous Quality Improvement (MS-CQI) Research Collaborative.

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Background: MS-CQI is the first randomized, multi-center, prospective, longitudinal, systems-level, improvement science research study for multiple sclerosis (MS). MS-CQI is a three-year study of system-level variation in performance outcomes, and leverages benchmarking to inform improvement using an informatics-enabled learning health system approach. MS-CQI collects eleven clinical electronic health record (EHR) outcome measures longitudinally, including MS treatment, all-cause emergency department utilization, and all-cause hospitalizations. We also collect demographic information and comorbidities.

Objectives: To describe Year 1 (baseline/pre-intervention) findings on system-level variation in selected clinical outcomes for individual sites, between sites, and for MS-CQI collectively.

Methods: Four MS centers in the U.S. are participating in MS-CQI: an urban academic center; a rural academic center; a rural community hospital; and a large urban private practice (N=5,000 persons with MS). We collected approximately 7,500 clinical measures abstracted from EHR data in Year 1 from nearly 3,000 clinical encounters. Demographic characteristics and longitudinal variation in measures did not vary significantly between sites. Encounter volume between centers was similar. We used ANOVA, multiple regression, and maximum likelihood estimation methods to conduct inferential analyses.

Results: Univariate analyses found significant differences ($p<0.05$) between sites for multiple clinical outcomes including exacerbations, disease modifying treatment, MRI utilization, emergency department utilization, and hospitalizations. Controlling for individual level factors, including comorbidities, significant site (system) level effects (with high performing center

specified as the referent group) were found for all-cause hospitalizations- with comparator sites demonstrating odds ratios (ORs) ranging as high as 2.4 (95% CI: 1.34, 4.4).

Conclusions: We found that significant geographic system-level variation in MS outcomes exists for all cause hospitalizations for people with MS followed by participating MS-CQI centers. Findings suggest that a focus on system-level variation and improvement may be needed to reduce all-cause hospitalizations for people with MS.

Disclosure: *Nothing to disclose.*

Keywords: Epidemiology of MS, System-level variation

(QOL07)

Relapse Rate Is Influenced By System-Level Variation: Year 2 Results of the Multiple Sclerosis Continuous Quality Improvement (MS-CQI) Research Collaborative

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Background: MS-CQI is the first multi-center improvement science research collaborative for MS, and includes a systems-level study of variation in MS outcomes. MS-CQI is a three year study that leverages benchmarking results to inform system-level improvement efforts targeting clinical outcomes using an informatics-enabled learning health system approach.

Objectives: Here we present relapse rate results for Year 1 (baseline/pre-intervention) compared to Year 2 (first year of intervention). We also describe system-level variation in relapse rate for individual sites, between sites, and for MS-CQI collectively.

Methods: We collect administrative data and eleven clinical electronic health record (EHR) clinical outcome measures longitudinally across four clinical MS care centers in the United States. We conduct statistical process control (SPC) analyses for benchmarking. Logistic regression and maximum likelihood estimation methods are used for inferential analyses.

Results: Four MS centers in the U.S. are participating: an urban academic center (n=1,000); a rural academic center (n=1,000); a rural community hospital (n=1,500); and an urban private practice (1,500), following a total N=5,000 persons with MS (PwMS). We have collected approximately 7,200 clinical encounter measures from EHR data in Year 1 and 10,000 in Year 2. Demographic characteristics and longitudinal variation in measures did not vary significantly between sites. For Year 1, center-specific proportions of PwMS with at least 1 relapse ranged 5-16.9%. Mean relapse rate varied significantly ($p<0.01$) across all centers. SPC analyses

demonstrate a MS-CQI reduction of relapse rate from 11.5% (Year 1) to 4.3% (Year 2). Two sites were below the MS-CQI average of 7% (3.3%, 6.3%) and two were above the average (8.5%, 10.3%). Controlling for individual factors and covariates, logistic regression analyses identified significant center level effects on relapse rate in Year 1, with comparator sites demonstrating ORs as high as 2.61 (95% CI: 1.8, 3.8).

Conclusions: MS-CQI has observed a significant reduction in population level relapse rate by 7.2% during the first year of QI intervention. We also found significant geographic system-level variation in MS relapse, suggesting that a focus on system-level variation and improvement may be needed to optimize outcomes.

Disclosure: *Nothing to disclose.*

Keywords: Comprehensive care and MS, Improvement Science in MS

(QOL09)

Living with Secondary Progressive MS: Results from an MS Coalition Survey

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Background: Many people diagnosed with relapsing multiple sclerosis (MS) will eventually transition to secondary progressive MS (SPMS). Until recently, only mitoxantrone had been approved by the U.S. Food and Drug Administration as a disease-modifying therapy (DMT) for this MS subtype. In 2018, however, the agency accepted an application for siponimod for treatment of SPMS. In anticipation of this drug's approval, the MS Coalition, a network of 9 independent MS organizations, surveyed people with SPMS to understand how the disease affects their lives and their experiences with and attitudes about DMTs. The survey was developed with the Institute for Clinical and Economic Review (ICER), which at the time was conducting a review of siponimod for use in SPMS.

Objectives:

1. To understand the challenges that people with SPMS face, including impacts on quality of life
2. To learn about current use of DMTs among people with SPMS and their perspectives on future DMTs that could be developed for SPMS

Methods: Representatives of MS Coalition member organizations and ICER developed this web-based survey, which was then disseminated by MS Coalition members whose constituents include people with MS.

Results: A total of 2263 respondents completed the full survey, and 2966 answered at least one question. Of those who participated in the survey, 51% reported being unable to work because of disability, 69% needed help with activities of daily living, and 86% used a mobility aid. About three-fourths chose "fewer available treatment options" (78%) and "decline in quality of life" (72%) as impacts associated with their form of MS. Regarding use of DMTs, 37% reported no current use, and 22% indicated that they were taking Ocrevus. The other DMTs included in the survey were each used by fewer than 10% of respondents. When asked to consider a hypothetical new drug for SPMS, respondents expressed broad interest in possible benefits the drug could provide, including prevention of brain atrophy and improvement in SPMS symptoms. Side effects and long-term risks topped the list of reasons respondents gave for why they might not stay on a new drug. In responses to open-ended questions about impacts on daily life and family, common themes related to isolation, burden on family members, stress, and loss of mobility.

Conclusions: Our respondents with SPMS described experiencing profound challenges, and their information provides insights into target areas of unmet need warranting continued therapeutic development.

Disclosure: *Nothing to disclose.*

Keywords: Disease-modifying treatments in MS, Management of activities of daily living in MS, MS and the caregiver/family

(QOL10)

Corticosteroid Pulse Therapy-Induced Hyperglycemia: Protocol for Capillary Blood Glucose Control

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Background:

Pulse therapy is the preferred therapy for treatment of Multiple Sclerosis (MS) outbreaks, which is a neurologic, demyelinating and inflammatory condition, with intermittent periods of outbreak-remission. The recommendation is corticosteroid doses (500 mg to 1g), every 3 to 5 days, administered at the hospital, as an inpatient, or as outpatient at an infusion clinic. The treatment reduces the inflammation during the outbreak phase of the MS and seeks to stabilize the crisis. Despite their side effects, the glucocorticoids (GC) are potent anti-inflammatories in the treatment of autoimmune pathologies. The GC block the entrance of glucose in the tissues and increase the proteolysis, decreasing their synthesis in muscles, skin, bones, connective tissue, fat cells, and lymphoid tissue. Before the pulse therapy, it is important to eliminate the possibility of an active infection and to always administer the antiparasitic to control possible infestations. Checking the blood pressure, body weight and capillary glucose are very important during the

infusion. Daily checks pre and post infusion are required as hyperglycemia may occur as an adverse effect of the therapy. The capillary blood glucose check is a blood test that gives immediate results about glucose concentration in the capillaries and the digital pulp.

Objectives: To describe a protocol for puncture site rotation for the capillary blood glucose test performed during pulse therapy.

Methods: A rotation pattern was established for the digital pulp punctures. The patient is directed to properly wash the hands and dry well. The nurse professional punctures the selected site on the right or left side of the distal phalanx of the finger chosen for the test, by alternating the puncture sites, and records the date, time, location and blood glucose value.

Results: not applicable

Conclusions: The introduction of a protocol for puncture site rotation, based on a simple code, assists in the communication between nursing professionals and promotes patient safety. The protocol allowed the participation and cooperation of the client thus establishing self-care.

Disclosure: *Nothing to disclose.*

Keywords: Comprehensive care and MS, Hyperglycemia, Nursing management in MS

(QOL11)

Natalizumab Is Associated with Improvement in Cognitive Processing Speed and Health-Related Quality of Life: Strive 4-Year Results

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Background: Multiple sclerosis (MS) negatively affects cognitive function and quality of life (QoL), interfering with a patient's ability to work, pursue leisure activities, and perform activities of daily living. Natalizumab is a highly effective treatment for patients with relapsing-remitting MS (RRMS) and has been associated with improved cognitive function and QoL.

Objectives: To examine 4-year, end-of-study cognitive processing speed and patient-reported QoL outcomes for natalizumab-treated patients with early RRMS.

Methods: STRIVE is a completed, 4-year, multicenter, observational, open-label, single-arm study of anti–JC virus antibody negative patients starting natalizumab <3 years after RRMS diagnosis. Cognitive processing speed was assessed by the Symbol Digit Modalities Test (SDMT). QoL was assessed via the patient-reported Multiple Sclerosis Impact Scale (MSIS-29). Outcomes were assessed annually. Changes from baseline were analyzed via a Wilcoxon signed-rank test.

Results: At baseline, patients in the intention-to-treat (ITT) population (N=222) had active disease with a mean of 1.4 (standard deviation [SD] 1.2) relapses in the prior year. Baseline mean SDMT score was 52.1 (SD 14.0). ITT patients showed improvements in SDMT score from baseline to year 1 (n=191; mean change from baseline [CFB]: 2.29 [95% CI 0.84, 3.73]; P=0.0006) with clinically significant improvements (ie, an increase ≥4 points) in year 2 (n=158; mean CFB [95% CI]: 4.3 [2.4, 6.2]; P<0.0001) and year 4 (n=174; mean CFB [95% CI]: 4.6 [2.9, 6.2]; P<0.0001). Patients with SDMT data at all time points (N=145) had clinically significant SDMT improvements in years 2–4 (mean CFB [95% CI]: year 2, 4.4 [2.5, 6.2]; year 3, 4.3 [2.9, 5.8]; year 4, 5.1 [3.4, 6.7]). ITT patients also showed significant improvements in MSIS-29 score starting in year 1 (mean CFB [95% CI]: physical, n=186; −3.9 [−5.8, −2.1]; P<0.0001; psychological, n=186; −1.7 [−2.8, −0.6]; P=0.0012) that were sustained through year 4 (mean CFB [95% CI]: physical, n=174; −4.7 [−6.9, −2.4]; P<0.0001; psychological, n=172; −2.6 [−3.9, −1.4]; P<0.0001).

Conclusions: Natalizumab treatment over 4 years was associated with a clinically significant improvement in cognitive processing speed as measured by the SDMT as well as improvement in patient-reported physical and psychological health. The potential for long-lasting (up to 4 years) improvement supports natalizumab's effectiveness in patients with early RRMS.

Support: Biogen.

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Keywords: Disease-modifying treatments in MS, Psychological issues and MS

(QOL12)

MS Patient Perspectives: Disease Education and Communication Needs

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Background:

Multiple sclerosis (MS) is a progressive neurological disease that can significantly impact quality of life (QoL). In recent years there has been a shift towards increased patient engagement to inform person-centered care. It is therefore important that people with MS (pwMS) are equipped with the knowledge needed for informed, shared decision-making and maintaining independence outside of a formal care setting.

Objectives:

This study aimed to identify unmet disease education and communication needs in pwMS to empower informed decisions, enable self-management and to maintain independence for as long as possible.

Methods:

In October 2018 a round table of patient representatives, pwMS, carers, and MS nurses agreed key themes associated with maintaining independence. In 2019, an official project Steering Group formed and two studies for pwMS were co-developed: a qualitative Online Patient Community activity and a quantitative online survey. The qualitative activity used Ipsos' Syndicated MS Online Patient Community (a consistent panel of pwMS), and the quantitative survey was recruited through the MS Trust monthly newsletter and Facebook group. Results were discussed and prioritized by the Steering Group.

Results:

Data were analyzed from 28 and 117 respondents with relapsing remitting MS (RRMS), from the Ipsos' Syndicated MS Online Patient Community and quantitative survey, respectively.

Maintaining independence was a key goal in the qualitative findings, however only 33% reported they felt that they could 'plan for the long term', and 21% said they set short-term/long-term goals for managing their MS.

Overall, 66% 'strongly/somewhat' agreed MS had prevented them from reaching their full potential and had a 'very/slightly negative' impact on QoL in terms of work (73%), social life (69%) and caring for family (57%).

Data from this study will explore the relationship between perceived MS knowledge, planning for the future, and impact on QoL.

Conclusions:

There is evidence of a negative impact of MS on QoL among participants of our study. This highlights the importance of understanding unmet needs in education, linking disease progression and impact on future QoL in the wider MS population.

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Keywords: Comprehensive care and MS, Management of activities of daily living in MS, Patient education

(QOL13)

MS Patient Perspectives: Impact on Employment

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Background:

Multiple sclerosis (MS) is a progressive neurological disease that can significantly impact quality of life (QoL). MS is typically diagnosed between the ages of 20 and 40, affecting individuals during critical employment years. Continued employment in people with MS (pwMS) has been shown to be associated with higher QoL and better disease management.

Objectives:

This study aimed to identify unmet communication and disease education needs in pwMS to empower informed decisions, enable self-management and to maintain independence for as long as possible. In particular, we sought to gain an understanding of the impact of MS on employment and highlight the main challenges for people to remain in work.

Methods:

In October 2018 a round table meeting of patient representatives, pwMS, carers, and MS nurses agreed key themes associated with maintaining independence. In 2019, an official project Steering Group formed and two studies for pwMS were co-developed: a qualitative online patient community activity and a quantitative online survey. The qualitative activity used Ipsos' Syndicated MS Online Patient Community (a consistent panel of pwMS), and the quantitative survey was recruited through the MS Trust monthly newsletter and Facebook group. Results were discussed and prioritized by the Steering Group.

Results:

Data were analyzed from 28 and 117 respondents with relapsing remitting MS (RRMS), from the Ipsos Syndicated MS Online Patient Community and quantitative survey, respectively.

Data from the quantitative survey revealed the following: 66% of respondents 'strongly/somewhat' agreed their MS had prevented them from reaching their full potential, and had an impact on QoL, with 73% of participants reporting that their MS had a 'very/slightly negative impact' on work life.

Overall, 69% were in full or part-time employment, with only 26% remaining in the same job, with the same hours, since their diagnosis. Data from this study will further explore the impact on work for pwMS.

Conclusions:

Findings from our study highlight the impact of MS on working life among participants. It is important to understand these issues in the wider MS population in order to prevent problems at work and future loss of work.

Disclosure: *Jessica O'Neill: Roche Products Ltd (jessica currently works for roche products ltd). Mavis G. Ayer: Biogen, Roche (sponsored delegate). Celgene, Merck, Novartis, Sanofi (consulting fee). Teva (sponsored education). Samantha R. Colhoun, Alison Thomson: Biogen, Novartis, Roche Products Ltd (consulting fee). Nicola Daykin: Roche Products Ltd (consulting fee). Brenda Hamill: Biogen, Novartis (sponsored delegate). Roche (consulting fee). Maria Fei: Roche Products Ltd (maria works for ipsos mori, who were funded by roche to undertake this research). Jordanne Florio: Roche Products Ltd (jordanne currently works for roche products ltd). Serena Pulcini: Roche Products Ltd (serena currently works for roche products ltd).*

Keywords: Disease education, Employment in MS, Management of activities of daily living in MS

(QOL14)

Determining the Relationship of Demographic and Clinical Variables with Fatigue in Multiple Sclerosis, Using the 5 Item Modified Fatigue Impact Scale (MFIS-5)

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Background: Fatigue is reported as one of the most prevalent and disabling symptoms in patients with Multiple Sclerosis (MS). The Modified fatigue impact scale (MFIS), is a self-reported tool that captures the degree of fatigue in relation to its impact on physical, cognitive and psychosocial functioning. A recent article by Rooney et al. has provided an improved understanding of the relationship of a variety of both clinical and demographic variables with the impact of fatigue on MS using the MFIS. To our knowledge, such a robust comparison has not been reported utilizing the shortened version, the MFIS-5.

Objectives: To determine the association between the impact of fatigue and demographics and clinical characteristics among persons with MS (PwMS).

Methods: This study was a secondary analysis of a cross-sectional study of 253 PwMS. Demographic variables included age, gender, race (white/nonwhite), smoking status (smoker/nonsmoker) and employment status (employed/unemployed). Clinical characteristics included disease duration (DD), body mass index (BMI), level of disability (patient determined disease steps [PDDS]), depression (center for epidemiologic studies-depression scale [CES-D]), cognitive processing speed (symbol digit modality test [SDMT]), and use of disease modifying therapy (DMT, [on a DMT/not on DMT]). All measures including fatigue impact (MFIS-5), were collected at a single visit. Spearman's correlation coefficient was used to determine the strength of the associations and Mann-Whitney U for comparison.

Results: The sample had a mean age of 48.6 yrs ± 11.6 (range: 20-73), DD of 12.3 yrs ± 8.7 (1-47), PDDS score of 2.7 ± 2.1 (range: 0-7), BMI of 28.9 ± 7.2 (range: 17.5-59.8) and MFIS-5 score of 9.6 ± 5.3 (range: 0-20). This sample was mostly female (75.9%), with relapsing MS

(94.5%), unemployed (51.1%), white (84.5%), nonsmokers (84.9%) and on a DMT (83.8%). Fatigue impact was moderately correlated with disability (r=0.571, p=0.000) and depression (r=0.552, p=0.000), and weakly associated to age (r=0.173, p=0.006) and SDMT (r=-0.297, p=0.000). No relationship was observed with DD or BMI. No difference was observed among dichotomized variables of gender, race, smoking status or use of a DMT. However, the impact of fatigue was found to be different (p=0.000) between those employed (median MFIS-5 score: 8) and unemployed (median MFIS-5 score: 12).

Conclusions: Our study demonstrates the impact of fatigue, as measured by the MFIS-5, is associated with higher disability, depression, age, and decreased cognition and is greater among those unemployed in PwMS. Given its ease of administration, the MFIS-5 serves as a practical measure for assessing the impact of MS fatigue in clinical settings. The current study provides increased understanding of its relationship with various clinical and demographic variables.

Disclosure: *Natasha Hameed, Jennifer A. Ruiz, Heather M. DelMastro: Nothing to disclose. Mary Bailey: Alexion, Biogen, Genentech, Genzyme, Novartis (speakers bureau). Celgene (consulting fee).*

Keywords: Comprehensive care and MS, Fatigue in MS

(QOL15)

Multiple Sclerosis Management and EDSS: A Great Start, but a Reason for Change Was Never so Apparent and Needed

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Background: Since the Expanded Disability Status Scale (EDSS) was pioneered by Dr. John Kurtzke in 1967, it has been incorporated into clinical trial measurements in People with Multiple Sclerosis (PwMS). When combined with reported relapse rates and MRI measurements of disease activity, EDSS has been the basis for approval of >15 Disease Modifying Therapies (DMT). No Evidence of Disease Activity (NEDA) has been proposed as the goal for optimizing DMT. EDSS remains critical for both NEDA and treatment. Use of a non-linear scale to measure disability can be problematic if there is great variability of PwMS within homologous EDSS defined disability levels. Functional ability reflects the combined impact of cognitive function, manual dexterity, ambulation and other factors. If the degree of variability of these “abilities” exceeds 20%, this scale would no longer be valid.

Objectives: To explore the combined variability of functional performance with groups of similar disability across important aspects of ability.

Methods: Retrospective review of prospective registry of PwMS that were evaluated by multidimensional computerized cognitive testing, digital gait analysis, and patient reported outcomes (PRO) for hand function that had simultaneous measurements of PDDS or EDSS.

Results: 258 PwMS 73% female, age 46+/-10 multi-domain computerized cognitive testing global summary score of 7 domains had adjacent EDSS overlap (0-2.5, 3-4.5, 5-6.5 and>7) of 65% and extreme EDSS group overlap was 42%. Accumulative cognitive impairment (#Cognitive domains impaired >1SD) was 72% across adjacent EDSS groups, and extreme EDSS group overlap was 38%. 254 PwMS 72% female, age 46+/-10 mean normalized velocity for preferred walking speed varied >20% within EDSS groups (A:0-2.5 (24%), B:3-4.5 (34%), C:5-6.5 (53%)) and overlapped >20% (AB: 29%, BC:25%). 783 PwMS 74% female age 49+/-11 completed PDDS and NARCOMS PRO for both hand function and tremor demonstrated variability >50% variability across all PDDS (0-1, 2-4, >4) and overlap >50% of adjacent PDDS groups and >32% across extreme PDDS groups.

Conclusions: While the EDSS greatly advanced the treatment of MS, the degree of variability of disease impact within and across disability groups warrants immediate abandonment of this measure of care. This should be replaced by clinical trials with objective patient centric multidimensional measures of disease impact to improve treatment selection and monitoring for progression.

Disclosure: *Mark Gudesblatt: Acorda, Amgen, Medtronic, Saol Therapeutics (speakers bureau). Biogen, EMD Serono, Novartis, Sanofi, Teva (contracted research). Jared Srinivasan, Olivia Kaczmarek, Taylor Drost, Lori Fafard, Kaitlyn Jaenicke, Daniel Golan, Timothy Fratto: Nothing to disclose. Barbara Bumstead, Marijean Buhse: Biogen, Genzyme (speakers bureau). Myassar Zarif: Acorda, Biogen, Genzyme, Teva (speakers bureau). Jeffrey Wilken: Biogen (contracted research). EMD Serono (speakers bureau). Genzyme (contracted research, speakers bureau). Cynthia Sullivan: Roche (contracted research). Gavin Giovannoni: AbbVie, Bayer-Schering, Biogen, Canbex, Eisai, Elan, Five Prime, Genentech, Genzyme/Sanofi, GlaxoSmithKline, GW Pharmaceuticals, Ironwood, Merck Serono, Novartis, Pfizer, Roche, Synthon BV, Teva (consulting fee). Multiple Sclerosis and Related Disorders (Elsevier) (serving as co-chief editor). UCB Pharma (grants).*

Keywords: Comprehensive care and MS, Equipment in MS, Natural history of MS

(QOL16)

A Coach Supported Standardized Approach for Quality Improvement (QI) in the Multiple Sclerosis Continuous Quality Improvement (MS-CQI) Research Collaborative

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Background:

MS-CQI is the first randomized, multi-center, prospective, longitudinal, randomized, systems-level, improvement science research collaborative for MS. MS-CQI is a three-year study of system-level variation in performance outcomes, and leverages performance benchmarking to inform improvement using an informatics-enabled learning health system approach. MS-CQI has three components: (1) collection and reporting of benchmarking data, 11 clinical outcome and 21 patient reported outcome measures; (2) a QI coach-supported QI intervention utilizing a standardized Tool Kit; and (3) a three-year, step-wedge randomized study to test the effect of QI versus control on MS health outcomes. Four MS centers are participating: urban academic center; rural academic center; rural community hospital; and a large urban private practice (N=5,000)

Objectives: Describe system readiness to engage in QI and characteristics of multiple sclerosis (MS) centers randomized to coach-supported QI intervention.

Methods: MS centers randomized to QI participate in site visits and regular meetings with the QI coach. Teams use MS-CQI benchmarking data, local level data and a standardized QI Tool Kit to develop their improvement theme and improvements. The QI coach conducts regular assessments of team QI knowledge, skills, attitudes, and readiness to engage in QI work at monthly intervals, including QI assessment scales (IHI Improvement Progress and QI Knowledge Application and Skills).

Results: MS-CQI is in Year 3. One center was randomized to QI in Year 2 (private for profit) of the study and 2 centers were randomized (one rural, one urban academic) in Year 3. Site teams have identified QI foci including, patient access, patient orientation, pre-visit planning, social work and behavioral health and emergency room utilization. The teams are showing progress in their QI culture and development- IHI Improvement Progress Scale scores have changed from initial score of 1.5 (Planning for the project has begun) to 3.5 (some improvements in measurements and outcomes and continuing to improve)

Conclusions: MS center teams randomized to intervention in MS-CQI have successfully engaged in the coach-supported QI intervention. Site readiness and capability assessments reveals a greater understanding of their QI needs and a standard and consistent approach to improvement suggesting an initial positive response to the intervention.

Disclosure: *Nothing to disclose.*

Keywords: Comprehensive care and MS, Nursing management in MS, Quality Improvement

(QOL18)

Does Participation in a Six-Week Mindfulness Course Improve Mood and Overall Emotional Wellness for People Living with Multiple Sclerosis?

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Background: People living with multiple sclerosis (MS) often experience emotional distress about the life they had prior to the diagnosis of MS and what that diagnosis means for their future. The Multiple Sclerosis Achievement Center (MSAC) conducts day wellness programs to address physical, cognitive and social well-being. Program activities include exercise, brain training, education, socialization, and community outings. As part of the MSAC program, members have the opportunity to participate in a six-week mindfulness course to address emotional wellness.

Objectives: To determine, through the use of patient reported outcomes (PRO), if members participating in the mindfulness course demonstrate improvements in mood and overall emotional wellness.

Methods: Members of the MSAC will be asked to complete 4 paper/pencil outcome measures in January 2020 as part of their annual participation in the MSAC's programs, including the Multiple Sclerosis Impact Scale-29 (MSIS-29), Multiple Sclerosis Self-Efficacy Scale- 10 item (MSSE), Godin Leisure-Time Exercise Questionnaire (GTLEQ), and Neuro-QoL (Anxiety, Depression, Emotion & Behavior, Positive Affect, Cognition, Ability to Participate, and Social Roles sections are used). Members will be offered the opportunity to participate in a professionally-facilitated six-week mindfulness course, starting in January 2020, to provide education, strategies, resources and emotional support to achieve what they need and/or want for the present moment. Participants of the mindfulness course will be asked to complete PRO measures upon completion of the course.

Results: One-year and two-year comparison data of PROs, from MSAC members, have indicated correlations between Self-Efficacy, Anxiety, Ability to Participate, and Positive Affect (per MSSE & Neuro-QoL). Additionally, increased MSIS-29 scores directly correlate with anxiety while inversely correlating with self-efficacy and GTLEQ. Mean scores of depression, reported from the Neuro-QoL, remained the same (x=48) over a two year reporting period. These comparisons did not specifically measure a member's participation in the mindfulness course.

Conclusions: Data collection and analysis will be completed for those members participating in the six-week mindfulness course. Analysis will include pre and post measures, as well as comparison with those not participating in the mindfulness course.

Disclosure: *Tiffany Malone, Lacey Sayre: Nothing to disclose. Brian Hutchinson: Biogen (speakers bureau).*

Keywords: Mindfulness

(QOL19)

The Mediterranean Diet and Fatigue, Depression, and Emotional Wellbeing in MS - a Study in Patient-Reported Outcomes

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Background: Multiple sclerosis (MS) is a chronic demyelinating inflammatory disease of the CNS and a leading cause of disability amongst young adults. It presents with a variety of neurologic symptoms, which can significantly affect the quality-of-life of affected individuals. Although no specific diet exists for MS, dietary factors show potential for beneficial effects on inflammation, neuroprotection and repair. Increased dietary quality has been associated with lower disability and symptom burden in MS. Various diets, including ketogenic, fasting, Mediterranean, and plant-based diets produced mixed results in studies. The Mediterranean diet (MD) is high in antioxidants, fiber, mono- and polyunsaturated fatty acids as it emphasizes higher intake of fish, olive oil, fruits and vegetables. Previous studies have shown the MD may be beneficial in risk reduction for cardiovascular diseases, type 2 diabetes, obesity, cognitive impairment and brain atrophy. Limited studies have researched the relationship between MS outcomes and MD adherence. Preliminary evidence suggests that a MD may be beneficial in the MS population as it may be associated with reduced fatigue, impact of MS symptoms, and disability. Early findings warrant further investigation on the impact of a MD on MS outcomes to provide more evidence on the relationship of this diet on fatigue, cognitive function, and emotional well-being in MS.

Objectives: To examine the relationship between adherence to the MD diet and fatigue, cognitive function and emotional well-being, as captured by validated patient reported outcomes in MS.

Methods: Subjects will be recruited, consented and enrolled from the University of Florida MS clinic. Adherence to the MD will be determined by using the validated 14-Item Mediterranean Diet Assessment Tool. Neuro-QOL questionnaires will score cognitive function and emotional well-being, while the validated Modified Fatigue Impact Scale will score fatigue. Data analysis will determine the relationship between adherence to the MD and fatigue, cognitive function and emotional well-being.

Results: Data collection is ongoing.

Conclusions: Diet is an important factor to consider in comprehensive MS care and may have significant impact on quality of life. We hypothesize that MD will be associated with improved fatigue, cognitive function, and emotional well-being scores; though further research will better characterize its impact.

Disclosure: *Aaron Carlson: Novartis Pharmaceutical (contracted research). Sanofi Genzyme (consulting fee). Jamie Bolling, Carley T. Rusch, Alison Kraus, Nicole Tester, Nicole Herndon, Carlos Vervloet Sollero, Tirisham V. Gyang: Nothing to disclose.*

Keywords: Complementary/alternative therapies in MS, Comprehensive care and MS, Nutrition and MS

Rehabilitation

(REH01)

Assistive Technology for Progressive Deficits in Communication and Access People with Advanced Multiple Sclerosis: Case Studies in Iterative Design

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Background: People with advanced multiple sclerosis (PwAMS; EDSS > 6.5) can experience dynamic and progressive changes in motor speech intelligibility, vocal projection, and upper extremity control and coordination which can interfere with access to typical expressive communication modalities (e.g., telephone & computer access). In most cases, assistive technology (AT) can be useful in supplementing or replacing these functions to promote effective communication with partners and caregivers to maximize functional communication independence with minimal need for caregiver assistance.

Objectives: Participants will have the opportunity to understand how PwAMS can maximize functional independence with appropriate and supported access to AT. Participants will recognize how increasingly mainstream and ubiquitous technology can be modified and interfaced with more customized AT to meet unique access challenges in the MS population. Participants will have a better understanding of how nursing and allied health/rehab disciplines can collaboratively support PwAMS to complete electronic ADL's even in the presence of severe motor disability.

Methods: This case series will describe the experiences of 3 PwAMS at the Boston Home, a specialized residence for individuals with advanced neurodegenerative disorders, who have benefited from using AT with ongoing customization and intervention to adapt the technology as appropriate to accommodate for MS-associated progressive motor, sensory, and cognitive deficits using currently available AT within the past 5 years. One individual will demonstrate

concepts of iterative design as motor access to augmentative communication devices deteriorated; another will illustrate accommodations to speech-recognition technology despite progressive dysarthria; the third highlights cumulative adaptations to nurse call and speakerphone access options to compensate for worsening hypophonia and quadriplegia in order to maintain contact with remote family and caregivers. Photos of the applied AT will illustrate how postural limitations and desire for wheeled mobility guided the decision-making process for selecting and modifying systems to meet the needs of the users. The roles of rehabilitation, nursing, and adaptive technology specialists in developing, modifying, and implementing appropriate iterations of communication AT in this particular care setting will be described as part of the interdisciplinary team caring for this cohort of PwAMS.

Results: Recommendations for providing caregiver education and eliciting feedback and considerations for designing, implementing, and adapting communication AT for PwAMS in other residential environments will be discussed. Outcomes in terms of satisfaction with AT access, services, and devices from PwAMS and caregivers will also be described using formal and informal assessment options.

Conclusions: N/A

Disclosure: *Alexander Burnham: The Boston Home (salary).*

Keywords: Comprehensive care and MS, Equipment in MS, Management of activities of daily living in MS

(REH02)

Predictors of Improvement in Respiratory Function Following Resistive Inspiratory Muscle Training in Advanced Multiple Sclerosis

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Background: Respiratory compromise in people with advanced MS (PwAMS = EDSS ≥ 6.5) worsens as the disease progresses and is a major cause of morbidity and mortality. There is evidence that exercise can improve respiratory muscle function in PwAMS even in later stages of the disease.

Objectives: It is not known if certain characteristics of PwAMS contribute to their ability to benefit from a respiratory exercise program. This study identified some possible predictive factors.

Methods: Thirty-eight subjects were recruited at a SNF specializing in care for PwAMS. Inclusion criteria were age > 18, MS diagnosis, and EDSS $\geq$ 6.5. The current study utilized a repeated measures within-subject design in which participants performed 3 sets of 15 repetitions of resistive inspiratory muscle exercises daily for 10 weeks using the Threshold Inspiratory Muscle Trainer (IMT). Demographics, number of comorbidities, body mass index (BMI), EDSS, and years post MS diagnosis were obtained at time of enrollment. Maximum inspiratory pressure (MIP) and maximum expiratory pressure (MEP) were obtained as measurements of respiratory muscle strength at several intervals over the 28-week duration of the study, including 10-week baseline phase, 10-week intervention phase, and 8-week retention period post-intervention. Progression of IMT resistance was adjusted weekly by the research team based on symptoms, rate of perceived exertion, and baseline MIP. Secondary outcomes assessed included fatigue (evaluated with MFIS-5) and cognitive processing speed (measured with oral version of the Symbol Digit Modalities Test (SDMT)).

Results: Correlation analysis of baseline characteristics with MIP change scores (MIP-CS) was performed to identify potential predictors of improvements in MIP for the regression analysis. Two separate linear regression models with MIP-CS and predicted values (MIP%-CS) as dependent variables were constructed. The regression model with BMI, fatigue (MFIS-5), and cognition (SDMT) as independent variables and MIP-CS as the dependent variable was significant ($F(3.25)=3.19$, $p=0.041$, $R^2=0.53$). SDMT was a significant predictor in the model ($p=0.035$) (higher SDMT scores significantly associated with better outcomes of IMT training); BMI as predictor approached significance ($p=0.056$). The regression model with BMI, MFIS-5, and SDMT as independent variables and MIP%-CS as the dependent variable was significant ($F(3.25)=3.19$, $p=0.027$, $R^2=0.55$). BMI was a significant independent predictor in the model ($p=0.029$), with higher BMI associated with worse outcomes with IMT training; SDMT as predictor approached significance ($p=0.053$).

Conclusions: Participant scores in BMI, MFIS-5, SDMT, and age/gender-adjusted MIP at baseline significantly predicted MIP-CS ($F(4.33) = 6.34$, $p = 0.001$, $R^2 = 0.44$, R^2 adjusted = 0.37). Factors such as age, gender, duration of disease, EDSS score, and number of comorbidities were not significant predictors of MIP-CS.

Disclosure: *The Boston Home (salary). Lisa Doyle, Min H. Huang, Donna Fry: Nothing to disclose.*

Keywords: Comprehensive care and MS, Equipment in MS, Respiratory intervention in MS

(REH03)

Rehabilitation of Dysarthria in Multiple Sclerosis

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Background: Introduction: Multiple Sclerosis (MS) can affect the speech motor system and result in dysarthria. The Lee Silverman Voice Treatment (LSVT-LOUD®) is an intensive behavioral treatment program to improve overall voice and speech functions in individuals with neurological diseases.

Objectives: The main goal of this study is to inspect the efficacy of LSVT-X treatment in MS patients.

Methods: Thirty four participants (RRMS relapsing remitting =16, SPMS secondary progressive =14, PPMS primary progressive =4), 27 female and 7 male, with ages ranging from 31 to 81 years, received the LSVT-X, administered twice a week in 1-hr sessions over 8 weeks. The evaluation was performed by three expert speech therapists. The auditoryperceptive analysis of their voices was carried out, based on the GRBASI scale. The acoustic analysis was also conducted by Praat software (version 6.0.50), considering the following measures: fundamental frequency, and voice intensity. Data were statistically analyzed to compare pre and post rehabilitation.

Results: Several signs and symptoms related to voice and speech were verified in different proportions and impacts on the intelligibility of verbal communication. Four altered domains have been identified: articulation (slow articulation, imprecise consonants), voice (pitch and intensity instability, impairment in vocal quality), respiration (decreased phonatory time, short cycles) and prosody (longer and frequent pauses, deficient loudness control). After treatment, there was improvement in parameters analyzed, dysarthria was attenuated and positive results were achieved.

Conclusions: In addition to conventional pharmacologic therapy, dysarthria treatment should be emphasized as part of a management plan focused on overall health and well-being, regardless of the type of MS, course of disease and manifestation of speech and voice symptom.

Disclosure: *Nothing to disclose.*

Keywords: TYPE NEW KEYWORD HERE

(REH04)

Daily Occupational Performance in Multiple Sclerosis

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Background: Introduction: Multiple Sclerosis (MS) is a chronic, inflammatory and degenerative disease that affects the central nervous system. Occupational performance is often compromised and negatively impacts daily activities and activities.

Objectives: To understand the perception of people affected by MS on occupational performance and identify the main difficulties in routine activities.

Methods: 55 people with MS participated, being 40 (73%) women and 15 (27%) men, aged between 27 and 60 years. The five major impairments in occupational performance were observed, according to the degree of importance, according to the Canadian Occupational Therapy Model (COTM), then the participants self-assessed their performances and satisfactions by means of a scale of 1 to 10 points.

Results: The analyzes revealed that participants considered their ability to perform routines and perform roles and tasks related to moderate to poor personal care, leisure and productivity.

Conclusions: Signs and symptoms of muscle weakness, fatigue, cognitive and visual changes and sensitivity were determinant to impair occupational performance appropriate to the needs and interests of the participants. The evaluation of occupational therapy and the rehabilitation of disabilities organized and facilitated the daily lives of people with MS.

Disclosure: *Nothing to disclose.*

Keywords: occupational therapy

(REH05)

Assessing the Benefits of Using Telehealth in Conjunction with a Fitbit to Improve Walking in Veterans with Multiple Sclerosis

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Background: Patients with multiple sclerosis often have limitations with mobility due to fatigue, weakness, and impairments with balance and coordination. Many of these patients decrease their activity and walking due to these limitations, which can lead to further deconditioning.

Objectives: The objective of this study was to examine improvements in walking distance and perceived impact of walking ability in patients with Multiple Sclerosis using a Fitbit in conjunction with telerehabilitation.

Methods: Currently 2 patients are enrolled in pilot with ongoing recruitment. Patients are asked for a self- perception of daily step count at evaluation. The 2 minute walk test and 10 meter walk test are administered at initial evaluation for baseline measures. Patients are given a Fitbit and asked to do their normal activity until the first telehealth session. At the first telehealth session the therapist views the patients walking log and establishes a weekly goal. Weekly sessions to

monitor and progress home walking program occur over telehealth. After 12 sessions of telehealth, the patient attends a clinic post program evaluation to obtain outcome measures. The patient is given the Fitbit to continue with program independently.

Results: To be determined

Conclusions: To be determined

Disclosure: *Nothing to disclose.*

Keywords: Equipment in MS, Management of activities of daily living in MS, Telehealth

(REH06)

Feasibility of Telehealth Rehabilitation for Veterans with Progressive Neuromuscular Disease

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Background:

Individuals who live in rural communities have difficulty accessing specialized medical services such as physical therapy. Individuals with progressive neurological diseases that do have access to physical therapy are limited to what is available in their community. Exercise is feasible and can improve fitness and improve quality of life for individuals with progressive neurological disease. Clinical Video Telehealth (CVT) provides these veterans with access to specialists for their condition and significantly reduces the energy and financial costs of traveling to specific appointments. Barriers exist whether an individual lives in a rural community or within a few miles of a health center. Utilizing CVT can eliminate these barriers and greatly improve adherence to a physical therapy rehabilitation programs. Finally, the ability to view an individual in their home environment gives providers the ability to problem solve physical challenges and safety issues that may be present in a person's home.

Objectives:

1. Extend specialty care from Neurology into Physical Medicine and Rehabilitation for Veterans with MS.
2. Determine the feasibility of the CVT devices in a variety of settings.
3. Decrease travel hours and costs.
4. Minimize caregiver time, burden, and other costs.

Methods:

There were 19 veterans evaluated during the study period. Eighteen of these veterans were diagnosed with multiple sclerosis and one of them was diagnosed with amyotrophic lateral sclerosis (ALS). Veterans were referred to PM&R physical therapy and evaluated by neurological clinical specialist. They were evaluated before and after the intervention period using standardized functional outcome measures. Follow up visits were scheduled at least 1x every week for 30 minute sessions and were re-evaluated every 30 days for up to 90 days. Veterans had the opportunity to extend their rehabilitation session for another 90 days if they were making improvements. Sessions took place with the clinical specialist in a private office with necessary rehabilitation equipment available for demonstration of exercises.

Results:

N=18, 18 had pre-intervention assessments, and 10 patients agreed to participate. 4 patients had a discharge visit where post-intervention measures were collected.

Total visits: 63

Travel Miles saved: 6770 miles

Travel Dollars Saved: $3,724

Conclusions:

Telehealth visits for patient with progressive neuromuscular disease such as multiple sclerosis and ALS can be effective and feasible in an outpatient setting. There were no adverse effects and this program resulted in a significant reduction in miles traveled and cost savings for veterans and the Veteran Health Administration. Barriers to adopting new technology were an issue for some veterans, and greater improvements were seen with those who incorporated new technology easily.

Disclosure: *Nothing to disclose.*

Keywords: Complementary/alternative therapies in MS, MS and the caregiver/family, TYPE NEW KEYWORD HERE

(REH07)

Systematic Review on Exercise Training As a Neuroplasticity-Inducing Behavior in Multiple Sclerosis

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Background: Exercise training is associated with improvements in physical fitness, walking mobility, balance, and possibly cognition in persons with multiple sclerosis (MS), perhaps based on neuroplasticity. However, it is difficult to characterize exercise training as a neuroplasticity-inducing behavior among persons with MS based on changes in functional outcomes alone, as neuroplasticity reflects true brain-behavior relationships.

Objectives: The current systematic review provided a critical evaluation of exercise training as a neuroplasticity-inducing behavior in persons with MS based on a well-established conceptual model. This involved prioritizing exercise training studies in persons with MS that included both functional and neuroimaging outcomes and further examined associations among these outcomes.

Methods: We performed an open-dated search of online scholarly databases in July 2019 using a targeted and comprehensive search strategy. In order to be eligible for full-review, papers had to be published in English and include the following components: (a) exercise training; (b) neuroimaging outcomes; and (c) functional outcomes (i.e., measures of physical fitness, walking mobility, balance, and/or cognition) in persons with MS. Acceptable study designs included randomized controlled trials (RCTs), single-group pre/post designs, and quasi-experimental designs. Four independent reviewers extracted relevant data from each eligible paper, including information on participant characteristics, exercise intervention characteristics, neuroimaging outcome characteristics, functional outcome characteristics, and pattern of study results.

Results: The literature search returned only 9 papers (involving 7 original interventions) that met eligibility criteria wherein inferences regarding neuroplasticity could be drawn, based on the inclusion of both neuroimaging and functional endpoints. Within those 9 papers, there is mixed evidence for exercise training as a neuroplasticity-inducing behavior in persons with MS.

Conclusions: There is insufficient data necessary to draw definitive conclusions on exercise as a neuroplasticity-inducing behavior in MS. Future research efforts might consider examining specific neural changes that would be expected to result from exercise prescriptions that are specifically designed to induce certain functional changes among persons with MS.

Disclosure: *Nothing to disclose.*

Keywords: CNS repair, Exercise , Imaging and MS

(REH08)

Aerobic Reserve in People with Multiple Sclerosis: Measurement and Correlates

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Background: The concept of aerobic reserve reflects the available potential energy to perform essential tasks to maintain independent living and is calculated by subtracting the energetic demand for activities of daily living from peak aerobic power. To date, the concept of aerobic reserve has not been applied in MS, and there are limited data on its measurement and correlates in this population.

Objectives: This study described the measurement and correlates of aerobic reserve in MS.

Methods: The sample included 23 people with MS who were fully ambulatory [median (range) Expanded Disability Status Scale (EDSS) = 3.5 (2.0)]. Participants completed a single session that included obtaining informed consent, EDSS examination, demographic questionnaire, as well as administration of the Symbol Digit Modalities Test (SDMT), Timed 25-Foot Walk Test (T25FW), 6-minute walk distance (6MWD), and a cardiopulmonary exercise test (CPET) performed on a treadmill (modified Balke protocol). Aerobic reserve was calculated by subtracting the person's steady-state VO_2 extracted during the first stage of the CPET from peak VO_2 obtained from the CPET.

Results: Twenty-one of 23 participants met criteria for providing a maximal effort during the CPET. The mean (SD) aerobic reserve was 9.5 (± 3.7) ml/kg/min. Aerobic reserve strongly correlated with peak VO_2 [mean (SD), 22.4 (±5.4) ml/kg/min], $r = 0.77$, $p < 0.01$. Aerobic reserve was positively correlated with SDMT raw score [mean (SD), 49.3 (±7.2)], $r = 0.45$, $p = 0.03$ and time to exhaustion in seconds on the CPET [mean (SD), 592.8 (±205.5)], $r = 0.63$, $p < 0.01$. Aerobic reserve was negatively correlated with resting heart rate [mean (SD), 79.4 (±11.5) bpm], $r = -0.50$, $p = 0.02$ and BMI [mean (SD), 29.6 (±5.8) kg/m^2], $r = -0.56$, $p < 0.01$. Aerobic reserve did not correlate with age, sex, EDSS, T25FW, or 6MWD.

Conclusions: Aerobic reserve can be measured during CPET in people with MS, and might have implications for understanding symptomatic and functional outcomes in people with MS.

Disclosure: *Nothing to disclose.*

Keywords: Aerobic Exercise Training, Complementary/alternative therapies in MS, Management of activities of daily living in MS

(REH09)

The Impact of Vascular Comorbidities on Perceived Functional Impact in Persons with Multiple Sclerosis

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Background: Persons with multiple sclerosis (PwMS) can have a number of comorbidities and secondary conditions, which can complicate care and negatively affect health-related quality of life. In particular, chronic vascular conditions, such as diabetes, hypertension, hyperlipidemia, and heart disease, have been associated with more rapid accumulation of irreversible disability in PwMS. However, little is known about the impact of co-occurring chronic vascular conditions on perceived functional impact in PwMS.

Objectives: To examine differences between PwMS with and without vascular comorbidity with regards to their self-reported functional impact.

Methods:

Participants (n = 257) were randomly selected PwMS who participated in the MS Characterization of Upper Extremity Functioning (MS-CUE) study. The MS Impact Scale (MSIS-29) was used to measure perceived physical and psychological impact on daily life, while the Functional Status Index (FSI) was used to assess functional performance in five domains: gross mobility, hand activities, personal care, home chores, and social/role activities. Due to non-normally distributed data, Mann-Whitney U analyses were conducted to examine differences between PwMS with and without a vascular comorbidity, with effect size reported as r.

Results: On average, PwMS were 48.72 ± 11.56 years old (0 - 73) and had MS for 12.40 ± 9.78 years (1 - 47), with a median Patient Determined Disease Steps (PDDS) score of 3 (0 - 7). A total of 112 of 257 (43%) PwMS had at least one co-occurring vascular condition, with hyperlipidemia (n = 72, 64.3%) and hypertension (n = 66, 58.9%) being the most common. PwMS with at least one vascular comorbidity reported higher levels of physical (r = -.29, p <.001) and psychological impact (r = -.16, p = .009), as well as more issues with gross mobility (r = -.28, p <.001), hand activities (r = -.17, p = .007), personal care (r = -.19, p = .002), home chores (r = -.24, p <.001), and social/role activities (r = -.24, p <.001).

Conclusions: PwMS with vascular comorbidity have worse perceived functional performance and physical and psychological well-being compared to PwMS without vascular comorbidity. These findings suggest that the presence of chronic vascular conditions in PwMS negatively impacts perceived functioning, which has important implications for provision of care and quality of life for PwMS. Future work unraveling the mechanism by which vascular comorbidity influences perceived functional outcomes warrants further evaluation.

Disclosure: *Elizabeth S. Gromisch, Heather M. DelMastro, Lindsay O. Neto, Jennifer A. Ruiz, Aaron P. Turner, Thomas P. Agresta, Albert C. Lo: Nothing to disclose. Gabriele C. DeLuca: Merck-Serono (contracted research). Novartis (speakers bureau). Sanofi-Genzyme (travel).*

Keywords: Management of activities of daily living in MS, Psychological issues and MS, Vascular comorbidity

(REH10)

Is Treadmill Walking Analogous to Overground Walking in Persons with Multiple Sclerosis?

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Background: Gait and walking impairment is a common finding in persons with multiple sclerosis (pwMS) and is often studied using a treadmill. However, studies in other neurologic conditions have questioned whether treadmill walking accurately represents overground walking. If it doesn't, it may be questionable whether gait research performed on a treadmill can be generalized to overground walking. Similarly, it may suggest that the use of a treadmill for clinical gait evaluation and intervention for pwMS may not be supported.

Objectives: The purpose of this study is to examine whether treadmill walking speed is similar to overground walking speed in pwMS. We hypothesized that treadmill walking speed would not be significantly different from overground walking speed in pwMS. If our hypothesis is correct, it will suggest that clinicians can be confident that use of a treadmill for the examination and treatment of gait and walking dysfunction is representative of overground walking. If our hypothesis is not supported however, it would suggest that clinicans who treat pwMS for gait and walking impairment should reconsider the use of a treadmill as a tool for evaluation and treatment.

Methods: 19 people with MS (11 women and 8 men; EDSS median 4.5, IQR 2.5, rage 2.0-6.5) performed an over-ground 2-minute walk test (2MWT) to determine their average walking speed, then were asked to walk at the same speed on a treadmill. Participants were given up to 10

minutes to familiarize themselves with the treadmill before trying to achieve their overground walking speed.

Results: Pearson correlations were utilized to examine the relationship between predicated walking speed (PWS) (based the mean walking speed during the 2MWT) and the actual walking speed (AWS) attained while on the treadmill. There was a positive correlation between AWS and PWS (r=.841 (r-squared=.707), n=19, p=.000). 70.7% of the variance in PWS could be predicted by the AWS. This, however, leaves 29.3% of the variance unexplained.

Conclusions: Although OW and TW may seem very similar; there are contextual differences in these activities that may limit generalizability between the two. Researchers should be cautious when generalizing outcomes in physical performance in PWMS measured during TW to expected performance in OW. Clinicians should also be cautious in expecting generalized training effects of TW on OW in PWMS. The walking techniques used on a treadmill may not be the same ones used for overground walking, and therefore treadmill walking may not generalize to overground walking.

Disclosure: *Nothing to disclose.*

Keywords: Complementary/alternative therapies in MS, Gait, Management of activities of daily living in MS

(REH11)

Tele-Rehabilitation Compared to Outpatient Rehabilitation for Patients with Multiple Sclerosis and Mobility Disorders

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Background:

Multiple Sclerosis (MS) is a multifocal disease of the central nervous system, often producing variable and long-standing symptoms that may lead to loss of function and disability. Access to specialized rehabilitation specialists may be limited by loss of mobility and distance from rural areas to outpatient rehabilitation centers.

This pilot study was undertaken to determine the feasibility of conducting a physical therapy (PT) guided tele-rehabilitation (TR) program for individuals with mobility deficits resulting from Multiple Sclerosis (MS). Data on mobility, quality of life (QOL), fatigue, and travel cost were examined. The TR group was then compared retrospectively to an outpatient based therapy (OP) group to review effect on mobility scores.

Objectives:

1. Determine if a TR program prescribed and monitored by a MS certified PT, delivered on a home, web-based platform is a feasible delivery technique for individuals with MS.
2. Identify if a TR program can improve access to a component of comprehensive MS care while reducing travel cost.
3. Examine changes to mobility scores for a TR program compared with an OP program to compare the effects of the two delivery options for individuals with MS.

Methods: Subjects with confirmed MS and mobility deficits were recruited from the MS Center of Excellence at UF Health Jacksonville for the TH group. Initial and final face-to-face examinations were performed by a board certified neurologist and a MS specialist PT. Subjects underwent eight weeks of PT guided TH utilizing the Jintronix® software platform and a kinetic tracking system. Subjects seen in OP by the same PTs performing the TH were selected by a chart review process from January 2018 through September 2019 with a diagnosis of MS (identified by a search of the practice's electronic database of the ICD 10 code G35). Subjects were selected for comparison based on duration of treatment and matching outcome measures completed. Data was then reviewed for effect on mobility and travel between the two groups.

Results: Eight participants completed the TR program. All TR subjects demonstrated improvement in either fatigue, QOL, or mobility measures. No adverse events were noted during or following completion of the program. The eight subjects saved a combined $8487.23 in projected travel costs. Results of measures between groups showed equivalence in terms of meeting minimal detectable change (MDC) for the outcome measures examined.

Conclusions: The eight-week TH program was feasible and safe for subjects with MS and mobility impairments. Compared to the OP group, the TH group demonstrated the same number of subjects meeting the MDC for the functional measures. Savings were superior in the TH group for travel cost and time. Further studies are needed to guide the design and establish the efficacy of tele-rehabilitation compared with outpatient rehabilitation programs.

Disclosure: *Nothing to disclose.*

Keywords: Comprehensive care and MS, Tele-rehabilitation

(REH12)

Management of Low Back Pain for Individuals with Multiple Sclerosis: A Case Series

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Background: Individuals with Multiple Sclerosis (MS) are often referred to a physical therapist (PT) for evaluation of immobility, pain, and functional impairment. These individuals may be referred during the diagnosis process, a relapse, or while clinically stable. Self-reported pain symptoms for individuals with MS can also be multifactorial and originate from several areas including symptoms of central, peripheral, orthopedic, or a combination of these origins. Therefore, the underlying diagnosis of MS may complicate the evaluation, treatment plan, and progression for individuals with MS presenting with orthopedic complaints- including low back pain (LBP). This retrospective case series presents four cases of individuals with MS that were referred to PT that also reported symptoms of LBP.

Objectives:

1. Identify special considerations for evaluation techniques, treatment modifications, and progression modifications specific to individuals with MS and LBP.
2. Initiate guidelines that should be considered when establishing a plan of care for similar individuals with MS in order to establish the most effective approach for functional improvement or stability.

Methods: All charts reviewed included subjects that attended the UF Health Jacksonville outpatient rehabilitation downtown location and were seen by the participating PTs from January 2018 through August 2019. Of the charts reviewed, four satisfied inclusion-exclusion criteria and are reviewed here. Charts were reviewed for PT plan of care, pain reports, and functional measures.

Results: In each case, subjects reported improvement or resolution in pain measures and also demonstrated improvement in functional measures examined. Specific interventions and functional measures were tailored for each patient and were found to vary due to individual differences in clinical presentation and differences in response to a given intervention.

Conclusions: The variability between subject presentation and complexity for individuals with LBP and underlying MS diagnosis were found to result in noted variance in treatment duration and approach between subjects. This points to the importance of thorough initial evaluation to include both neurological and orthopedic standard of care. The evaluation ensures an appropriate plan of care for individualized treatment as well as identification of potential barriers to progression of treatment. As MS is a progressive condition, it is important to educate and train patients in ways to self-manage their musculoskeletal pain and functional deficits once an appropriate treatment plan has been established. Further research is needed to establish specific outcome measures and screening tools to identify individuals that will best benefit from outpatient PT directed toward the impairment of LBP. The types of assessments and treatments reviewed in these cases may facilitate improved identification and standardization for these individuals.

Disclosure: *Nothing to disclose.*

Keywords: Comprehensive care and MS, Physical therapy

(REH13)

Predicting Fall Risk in Persons with Multiple Sclerosis Utilizing the 12-Item Multiple Sclerosis Walking Scale

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Background: Evidence suggests that 50-80% of persons with Multiple Sclerosis (PwMS) have difficulty walking and impaired balance, with half of them falling at least once a year. Falls can lead to increased risk of injury and fear of falling, which may further impair a person's function. Studies have previously shown that patient-reported outcomes (PRO's) predict PwMS' risk of falling but small sample sizes and variable cut-off scores have limited generalization of the findings.

Objectives: To determine the predictive value of a cut-off score for the 12-Item Multiple Sclerosis Walking Scale (MSWS-12) to identify PwMS with greater fall risk.

Methods: A total of 135 PwMS were included as part of a preliminary analysis of an ongoing, larger cross-sectional study in which the MSWS-12 and frequency of falls (self-reported over past 6 months) were collected. PwMS were designed as "faller" if they had >1 fall in the past 6 months. Descriptive statistics were used to describe the clinical characteristics of the fallers (n=82) and non-fallers (n=53) (age, gender, disease duration, use of assistance, and Patient Determined Disease Steps; PDDS). Clinical characteristics and MSWS-12 scores of the faller and non-faller groups were compared. A Receiver Operating Characteristic (ROC) curve was

used to estimate the classification accuracy of the MSWS-12. Optimal cut-off scores were calculated using the Youden index and sensitivity and specificity were calculated.

Results: There were no differences in age, gender, or disease duration between fallers and non-fallers. Fallers had higher median PDDS scores (3; 0-6 versus 1, 0-6; ($p< 0.01$)) and higher median MSWS-12 scores (67.5 versus 38.3; $p<0.001$) than non-fallers. Fallers were more dependent on assistive devices compared to non-fallers ($p<0.01$). The MSWS-12 cutoff score for fallers was ≥45.83 (Youden index: 0.46), with a sensitivity of 78.1%, specificity of 67.9% and a classification accuracy of 76.7% to detect fallers.

Conclusions: MSWS-12 was found to be predictive of fall risk in PwMS with a cut-off score much lower than previously reported. These findings indicate a lower threshold of the MSWS-12 score may help clinicians identify PwMS at greatest fall risk so that appropriate fall risk prevention interventions may be implemented.

Disclosure: *Heather M. DelMastro, Elizabeth S. Gromisch, Helen Dawes, Anton Pick, Jennifer A. Ruiz: Nothing to disclose. Gabriele C. DeLuca: Merck-Serono (contracted research). Novartis (speakers bureau). Sanofi-Genzyme (travel). Robert Krug: Novartis (contracted research).*

Keywords: Comprehensive care and MS, Falls

(REH14)

The Impact of Lower Limb Strength on Walking in Persons with Multiple Sclerosis: A Preliminary Analysis

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Background: Persons with MS (PwMS) report weakness and walking difficulty as some of their most disabling symptoms. Lower limb (LL) weakness is prevalent in PwMS and is associated with more significant disability, impaired balance, and increased difficulty walking. However,

limited research exists describing the relationship between strength of specific LL muscle groups and walking in the same cohort.

Objectives: To determine the impact of dominant (D) and non-dominant (ND) LL strength on Patient Reported Outcomes (PROs) and objective walking outcome measures in PwMS.

Methods: A cross-sectional sample of PwMS (n = 137) derived from a larger, ongoing study was used. The following walking measures were collected at a single visit: 12-item MS Walking Scale (MSWS-12), Timed 25 foot walk (T25FW), and D and ND Stride Length (StrL), Step Length (SL), and Double Support Time (DStime). Isometric peak torque of Hip extension and flexion (HExt; Flex) Knee extension and flexion (KExt; Flex), Ankle plantar and dorsiflexion (APF; DF), and Hip abduction (HAbd) were also collected. Descriptive statistics were performed (age, gender, disease duration and disability level: Patient Determined Disease Steps; PDDS) and a correlational analysis was used to determine the strength of the association of walking to strength in muscle groups.

Results: The MS cohort had a mean age of 51.4 yrs (range: 21-75), disease duration of 14.5 yrs (range: 0.3-40.0), and median PDDS of 2.5 (range: 0-7), with 74.1% being female. All muscle groups were correlated with SL and StrL, and inversely correlated with T25FW, MSWS-12, and DStime. Strong associations were observed between D HFlex and StrL (D: r=.621,p <0.001; and ND: r=.636,p <0.001), D HFlex and ND SL (r=.608,p <0.001), ND KFlex and StrL (D: r=.610,p <0.001; and ND: r=.622,p <0.001), ND HAbd and ND SL (r=.640,p <0.001) and ND HAbd and StrL (r=.605,p <0.001). Weak to moderate correlations (r = ± .190 to .599, p<0.05) were found for all remaining strength and walking measures assessed.

Conclusions: All LL muscle groups (HExt, HFlex, KExt, KFlex, APF, ADF, and HAbd) were associated with the PRO (MSWS-12) and objective walking variables (T25FW, gait parameters: StrL, SL, and DStime) collected. These findings suggest that strength training interventions of these muscles may improve walking in PwMS. Importantly, this study improves understanding of the relationship between different major LL muscle groups with both walking performance and perceived difficulty walking in PwMS.

Disclosure: *Heather M. DelMastro, Helen Dawes, Anton Pick, Jennifer A. Ruiz: Nothing to disclose. Gabriele C. DeLuca: Merck-Serono (contracted research). Novartis (speakers bureau). Sanofi-Genzyme (travel). Robert Krug: Novartis (contracted research).*

Keywords: Comprehensive care and MS, Walking

(REH15)

The Effects of Intermittent Versus Continuous Walking on Distance to Fatigue in Persons with Multiple Sclerosis

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Background: Diminished walking endurance is common in persons with MS (PWMS). Previous studies have shown that PWMS walk farther in 6 minutes when using intermittent walking (IW) [i.e. with interspersed rest breaks] than with continuous walking (CW), but it is unknown whether PWMS can walk greater distances or longer duration when using IW for periods of longer than 6 minutes.

Objectives: The purpose of this study is to compare distance and time walked on a treadmill at a fixed velocity utilizing IW or CW. We hypothesized that PWMS would be able to walk greater distances and for longer duration when walking intermittently than when walking continuously. If our hypothesis was correct, it would indicate that persons with MS can increase the total distance that they walk before being limited by fatigue using intermittent as opposed to continuous walking training.

Methods: A randomized crossover design was used. Participants were randomized into two order groups: IW then CW, or CW then IW. The IW condition included alternating 30 seconds of walking and 30 seconds of seated resting. The CW condition consisted of continuous walking. Participants wore an overhead harness for safety. Baseline walking speed was determined with a 2-minute walk test (2MWT). Participants walked at the fastest pace up to the 2MWT speed until they either lost their balance or asked to stop. Walking time (WT) and walking distance (WD) were recorded. After one week, participants returned and performed the crossover condition.

Results: 19 subjects (EDSS 4.7±1.4,10 female) compoleted the study.,Participants had significantly longer WD in the intermittent condition than in the continuous condition (1575.4ft SD± 498.4 vs 1035.9ft SD± 356.2,P=.028). IW enabled participants to walk at best-pace for greater distances than CW.

Conclusions: These findings further support the use of IW training to improve walking endurance in pwMS. Adding rest breaks during endurance training enabled participants in this study to walk farther and longer, increasing the "dosage" ofthe walking activity. Comparative effectiveness studies should be conducted to determine whether IW training is superior to the traditional model of CW training to improve walking endurance. In PWMS, greater walking distance can be achieved with intermittent walking than with continuous walking, suggesting that greater walking endurance gains can be made in these patients using this approach

Disclosure: *Nothing to disclose.*

Keywords: Complementary/alternative therapies in MS, Gait, Management of activities of daily living in MS

(REH16)

The Effects of Cooling Vests on Gait Fatigability in Persons with Multiple Sclerosis

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Background: Gait dysfunction is a ubiquitous and multifactorial finding in persons with MS (pwMS). A major reason for gait dysfunction in pwMS is objective fatigability (OF), characterized by progressive worsening of gait parameters over the course of a walk. Although OF is also multifactorial, it is presumed to be due in large part to MS thermosensitivity, where increased heat leads to decreased conduction through demyelinated nerves. Prolonged exercise such as long walks can lead to increased core temperature in pwMS, and therefore lead to progressive worsening of gait over the course of the walk. An intervention to prevent core temperature rise could limit OF during gait in pwMS.

Objectives: The purpose of this study was to investigate whether the use of a commercially available cooling vest would result in decreased OF of gait in pwMS. We hypothesized that wearing the vest for 30 minutes prior to a 6-minute walk (6MW) would result in less evidence of gait fatigability in persons with MS when compared to performing the 6MW without prior cooling. If our hypothesis is correct it will suggest that persons with MS who experience gait fatigability can mitigate this by the use of cooling garments.

Methods: A randomized crossover design is being used. Ambulatory patients with a dx of MS are randomized into a cooled (C) and uncooled (U) condition. Cooling is accomplished by the wearing of a commercially available cooling vest for 30 minutes while seated. The (U) condition is sitting for 30 minutes without wearing the vest. Immediately after the 30 minutes, subjects perform a 6-minute walk test (6MWT). Objective fatigability is measured by comparing the speed of the walk in the 1st minute to the speed of the walk in the 6th minute. Subjective fatigue is measured using the Visual Analog Scale of Fatigue (VASF). Data collection began fall of 2019 and will conclude Winter of 2020.

Results: To date, 5 subjects, (EDSS4.4) have completed the study. Due to the small sample size, only descriptive statistics are reported. Mean 6MWT distance higher in the cooled condition (1137.3') than in the uncooled condition (1087.9'). Mean differences between the distance walked in 1stminute and 6th minute was less in the cooled condition (-1.6') than in the uncooled (-12.4'). Subjects experienced less subjective fatigue as measured by the VASF in the cooled condition (7.4mm), than in the uncooled(13.8mm).

Conclusions: These findings, although preliminary, support our hypothesis that cooling may diminish OF of gait in pwMS and thereby improve gait endurance. Once we have achieved an adequate sample size a more in depth analysis will be performed. If our hypothesis is then reaffirmed, it will suggest that the use of a comercially available cooling vest may decrease the impact of fatigue on fait in pwMS.

Disclosure: *Nothing to disclose.*

Keywords: Equipment in MS, Gait fatigue, Management of activities of daily living in MS

(REH17)

A Combination of Core Exercise and Balance Based Torso Weighting for Women with Multiple Sclerosis

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Background:

Multiple Sclerosis (MS) is a neurodegenerative disease that often results in fatigue and balance and walking impairment. Core exercise has been shown to reduce fatigue, and improve balance and walking in people with MS. However, no studies have investigated the effects of a combination of core exercise and Balance Based Torso Weighting.

Objectives:

The purpose of this study was to investigate whether the combination of BBTW plus core exercise leads to greater improvement in self-reports of fatigue, balance confidence and walking ability compared to core exercise alone in women with MS.

Methods:

Eighteen women with MS (EDSS 3.0-5.0) were randomly assigned to one of two groups: core exercise (CE) or BBTW plus core exercise (BBTW + CE). Subjects completed three questionnaires at baseline and after a six-week intervention period: Modified Fatigue Impact Scale (MFIS), Activities Specific Balance Confidence Scale (ABC Scale) and the MS Walking Scale (MSWS-12). All subjects participated in a Pilates-based CE program once a week with a Physical Therapist along with a daily home exercise program. In addition to the CE, one group also participated in the BBTW protocol. This involved fitting subjects with a vest worn on the torso and application of small weights to the vest at baseline followed by biweekly sessions to adjust weights and gradually increase wearing time up to 6 hours daily.

Results:

Following the six-week intervention period, both groups demonstrated positive change indicating improvements in self-reported fatigue, balance confidence, and walking ability. The percent change for each measure was as follows: MFIS: CE group = 14.1% decrease, BBTW + CE group = 19.9% decrease; ABC Scale: CE group = 9.7% increase, BBTW + CE group 15.6% increase; MSWS-12: CE group: 11.9% decrease, BBTW + CE group = 19.3% decrease. Despite these improvements, none of the change in scores exceeded the MDC_{95} estimates for each measure (MFIS = 49%, ABC = 20%, MSWS-12 = 53%).

Conclusions:

Core exercise with or without BBTW led to decreased self-perceived fatigue and improved balance confidence and walking ability, however, the percent change for both groups did not exceed MDC_{95} estimates. The percent change in perceived fatigue, balance and walking was greater in the BBTW + CE group. The balance wear vest may provide individuals with added truncal proprioceptive input and recruitment of core stabilizers, however, the mechanism of improvement needs to be further investigated.

Disclosure: *Nothing to disclose.*

Keywords: Complementary/alternative therapies in MS, Core Exercise

(REH21)

Impact of Restless Legs Syndrome Severity on Cognitive Function in Adults with Multiple Sclerosis and Restless Legs Syndrome

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Background: Restless legs syndrome (RLS) is a sleep disorder present in as many as 26% of persons with multiple sclerosis (PwMS) and may exacerbate many of the symptoms and consequences of MS, including cognitive function. Additionally, RLS symptoms often impair sleep quality, which could further exacerbate the neuropsychological symptoms associated with MS.

Objectives: The present study examined the relationship among RLS severity and cognitive impairment in adults with MS and RLS.

Methods: Participants with MS were screened for RLS using the Cambridge-Hopkins Restless Leg Syndrome Short Form Diagnostic Questionnaire. Participants attended one session wherein a rater performed an examination for scoring the Expanded Disability Status Scale(EDSS) and

participants completed the International Restless Legs Syndrome Study Group Sale(IRLS), the Pittsburgh Sleep Quality Index(PSQI), and the Epworth Sleepiness Scale(ESS) followed by the Brief International Cognitive Assessment for Multiple Sclerosis battery consisting of the Symbol Digit Modalities Test(SDMT), California Verbal Learning Test-II(CVLT-II), and Brief Visuospatial Memory Test-Revised(BVMT-R).

Results: All participants (N=22) had RLS (mean IRLS=20.4; SD=6.1). Nonparametric bivariate correlations indicated strong, negative associations between scores from the IRLS and CVLT-II (ρ= ─0.627;p<0.01), BVMT-R (ρ= ─0.608;p<0.01), and years of education(ρ= ─0.632;p<0.01). There were no significant associations among scores from the IRLS and the SDMT, PSQI, or ESS. We performed two multivariate linear regressions with forward stepwise selection wherein we regressed scores from (1)CVLT-II on IRLS scores and (2)BVMT on IRLS scores in Step 1, and included variables that were significantly correlated with cognitive scores and IRLS scores in bivariate correlation analyses in Step 2 (i.e., years of education). IRLS scores significantly predicted CVLT-II (R^2=0.398) and BVMT-R performance (R^2=0.371); however, the relationship with BVMT-R performance was attenuated by including years of education (ΔR^2=0.144).

Conclusions: Our findings suggest that worse RLS severity could contribute to worse immediate verbal recall and memory and worse immediate visual recall and visuospatial memory in PwMS. Additional research is necessary to explore mechanisms that may underlie this association. If a causal pathway exists, diagnosis and treatment of RLS symptoms may offer new opportunities to reduce cognitive impairment in adults with MS.

Disclosure: *Nothing to disclose.*

Keywords: Psychological issues and MS, Sleep and MS

(REH22)

Utilization of Therapy Services Among Patients with Multiple Sclerosis

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Background: Multiple Sclerosis (MS) is a chronic, progressive neurologic disease estimated to be affecting nearly one million individuals in the United States. Common symptoms of MS include pain, impaired mobility or activities of daily living and fatigue, among many others. The use of rehabilitation in all settings has been shown to improve symptoms and function while helping to minimize disability.

Objectives: The purpose of this study was to examine the current usage of various rehabilitation services in the Kentucky area and understand barriers to rehab among patients with MS. A secondary objective was to identify areas in which patients require additional education related to managing their disease.

Methods: Eighty-nine participants completed a voluntary online survey which included nineteen questions about their disease and experiences with being referred to various types of rehab. Additional questions were asked about their knowledge, beliefs and any barriers related to rehab. Surveys were completed in Survey Monkey and results analyzed. Although the sample size was small, important information about therapy usage was gathered during this survey.

Results: Over half of participants are not participating in regular exercise, despite current literature that shows the benefits of exercise. Approximately one third of individuals surveyed are unaware of the benefits of various types of rehabilitation. Half of the participants have plans to make changes to either their diet or exercise programs over the next year. Around fifty percent of participants expressed interests in learning more about nutrition, supplements, exercise, stress management and stretching. These results highlight the need for continued patient education regarding management of MS symptoms.

Conclusions: Despite significant research that indicates the benefits of therapy for patients with MS, there continue to be many patients that have not been referred to skilled therapy services. Furthermore, most patients are interested in obtaining additional information related to managing their disease, which could be addressed by a comprehensive rehabilitation team.

Disclosure: *Nothing to disclose.*

Keywords: Complementary/alternative therapies in MS, Comprehensive care and MS, Management of activities of daily living in MS

(REH23)

Proximal Movement Compensations Are Related to Muscle Function and Walking Capacity in People with Multiple Sclerosis

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Background: Distal lower extremity movement compensations are associated with muscle weakness and mobility limitations in people with multiple sclerosis (MS), however less is known about pelvis and trunk compensations during walking.

Objectives: To 1) compare differences in pelvis and trunk kinematics during walking between participants with MS and a control group, and 2) determine associations of trunk and pelvis kinematics with muscle function, spatiotemporal parameters, and walking capacity in the participants with MS.

Methods: In this cross-sectional study, 20 people with MS (Expanded Disability Status Scale 1.5 to 5.5) and 10 people with comparable age and sex (CTL) underwent three-dimensional gait analysis. The primary kinematic variables of interest were frontal and sagittal plane pelvis and trunk angular displacement during the stance period of walking. All participants also underwent muscle function assessments (hip and trunk strength and endurance), and walking capacity measures (Timed 25-Foot Walk – T25FW, 2-Minute Walk Test – 2MWT).

Results: Compared to the CTL group, the MS group had significantly greater sagittal plane trunk and pelvis angular displacement for both the stronger ($p = 0.031$) and weaker ($p = 0.042$) sides; less frontal plane trunk and pelvis angular displacement for both the stronger ($p = 0.008$) and weaker ($p = 0.024$) sides; and more sagittal plane trunk angular displacement for the stronger side ($p = 0.047$) during stance phase. There were low-to-moderate correlations in the MS group for sagittal plane pelvis angular displacement with trunk flexion endurance ($r = -0.369$, $p = 0.019$); and frontal plane pelvis angular displacement with lateral trunk flexion strength ($r = 0.353$, $p = 0.030$), step length ($r = 0.529$, $p < 0.001$), stance time ($r = -0.433$, $p = 0.005$), T25FW ($r = 0.496$, $p = 0.001$), and 2MWT ($r = 0.582$, $p < 0.001$).

Conclusions: In people with MS, movement compensation at the pelvis during walking, particularly decreased frontal plane motion, was associated with worse walking capacity, muscle function, and spatiotemporal parameters. Future studies may consider targeting proximal muscle function to improve walking outcomes in people with MS. Rehabilitation clinicians may consider evaluation of proximal muscle function and gait compensations when planning rehabilitation interventions to improve walking capacity in people with MS.

Disclosure: *Mark M. Manago, Paul Kline, Cory Christiansen: Nothing to disclose. Enrique Alvarez: Actelion, Biogen, Celgene, EMD Serono, Genentech, Genzyme, Novartis, Teva, and TG Therapeutics (consulting fee). Biogen, Genentech, Novartis, and Rocky Mountain MS Center (contracted research).*

Keywords: rehabilitation in MS

(REH24)

Effects of a Weight Based Training Program on Bone Density, Cognition, and Quality of Life of Multiple Sclerosis Patients

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Background: Multiple Sclerosis (MS) is a chronic neurodegenerative disease caused by the lesion forming demyelination of the Central Nervous System. Some of the issues associated with Multiple Sclerosis include cognitive impairment, increased mental and physical fatigue, and decreased bone mineral density. Utilizing different variations of exercise is a common practice in the care for patients diagnosed with Multiple Sclerosis. It has been supported that there is a

positive impact associated with exercise and the long-term progression of functional limitations and quality of life measures in MS patients.

Objectives: Patients with Multiple Sclerosis have lower bone mineral density and a higher prevalence of osteoporosis. Physical activity has had a positive effect in bone health of MS patients. The primary purpose of this study is to investigate if there is a correlation between weekly body weight exercise and bone density in MS patients. Cognitive functioning and psychological well-being have also been shown to improve through the intervention of regular exercise. Additionally, cognitive and quality of life measures will also be investigated as part of this study**.**

Methods: This study will enroll a total of 25 patients. Patients eligible for the study are between the ages of 40-55, diagnosed with MS, and have an EDSS score below 5.5. Each patient will receive a baseline dual energy X-ray absorptiometry (DEXA) scan, a verbal Symbol Digit Modalities Test (SDMT) and a Multiple Sclerosis Impact Scale (MSIS-29). Following the baseline visit, patients begin a six-week body weight exercise program. The program consists of one thirty-minute group session, under trained physical therapist supervision, and one video guided at home session for a total of two sessions per week. Upon completion of the training program, each patient completes a midpoint SDMT and MSIS-29. An endpoint DEXA scan, SDMT, and MSIS-29 are conducted 8 weeks after the completion of the training program. Statistical analysis will be conducted for potential changes in bone density values, SDMT scores, and MSIS-29 physical and psychological scores.

Results: To date, 4 patients completed, 5 patients dropped, 4 patient enrolled/awaiting enrollment. Data is being collected and further analysis is required.

Conclusions: Thus far patients have reported positive experiences but until analysis, no conclusions can be made or supported with regard to bone density and cognitive effects.

Disclosure: *Mary Ann Picone: Biogen Inc. (speakers bureau).*

Keywords: Body weight exercise for MS, Complementary/alternative therapies in MS, Management of activities of daily living in MS

(REH25)

Orchestrating a New Path for MS Rehabilitation: Empowering Patients through Both Physical and Music Therapies

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Background: Although disease-modifying therapies (DMTs) are available for multiple sclerosis (MS) to delay disability progression and reduce relapses, as MS progresses, additional support and management of symptoms become increasingly important.

Objectives: To assess the role of nonpharmacological therapies, focusing on physiotherapy (PT) and music therapy (MT) that can lead to improvements in most of the physical and psychosocial domains that are negatively impacted in patients with MS.

Methods: MEDLINE was searched without date restriction to identify studies on the efficacy of PT and MT in MS. A panel of PT and MT experts was convened to identify important themes and research studies.

Results: PT can lead to improvements in mobility and balance. A review of 16 randomized controlled trials showed that treadmill training three times per week for 8 weeks improved walking endurance by 26.5 m from baseline in patients with MS. PT can also provide clinically meaningful improvements in fatigue, health-related quality of life (HRQoL), mood and cognition. In a group of 20 patients with MS who performed high-intensity resistance training twice a week for 12 weeks, patients achieved statistically significant reductions in anxiety ($p=0.002$), depression ($p=0.019$) and fatigue ($p=0.001$). Likewise, MT can improve physical symptoms and HRQoL in MS. In a trial comparing rhythmic-cued motor imagery, metronome-cued motor imagery and no intervention, patients in the two intervention groups could, respectively, walk a mean of 62.1 m and 60.9 m further after 4 weeks vs baseline; the mean change in the no intervention group was −17.1 m. Significant improvements in HRQoL measures were also seen in both intervention groups vs the no intervention groups for physical function, general health perception, vitality, social function and mental health ($p<0.05$).

Conclusions: While DMTs aim to reduce disability progression and inflammatory activities in MS, additional nonpharmacological therapies are an important adjunct for managing daily life with MS, particularly in improving or maintaining mobility, cognition and other functional systems. Current studies regarding the use of PT and MT in MS indicate these are highly beneficial tools in delaying the loss of both fine and gross motor skills, improving overall well-being and psychosocial health factors and, ultimately, preserving HRQoL. Further research on combined PT and MT interventions may further improve outcomes in MS.

Disclosure: *Megan Weigel: Acorda, EMD Serono, Mallinckrodt Pharmaceuticals (speakers bureau). Biogen Inc., Celgene Corporation, Inc. (consulting fee). Novartis Pharmaceuticals Corporation, Sanofi Genzyme (consulting fee, speakers bureau). Renee Fleming, Brian Hutchinson, Wendy L. Magee: Novartis Pharmaceuticals Corporation (consulting fee). Wendy Su: Novartis Pharmaceuticals Corporation (salary).*

Keywords: Complementary/alternative therapies in MS, Comprehensive care and MS, Management of activities of daily living in MS

(REH26)

Improving Quality of Life Using an End-Effector Robotic Rehabilitation Approach in Progressive Multiple Sclerosis

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Background: Progressive multiple sclerosis (MS) is characterized clinically by gradual disease progression and accumulation of neurological disability, independent of relapses. Rehabilitation has been recommended as a means to reduce disability and restore function. High quality evidence supporting progressive MS rehabilitation is limited. An end-effector robot-assisted gait trainer (RAGT) addresses many of the limitations of therapist-assisted gait training while providing an environment for regaining mobility and independence.

Objectives: The objective of this study was to establish the safety and feasibility of RAGT and determine its impact on movement capacity, fatigue, and quality of life in patients with progressive MS.

Methods: Single-blinded, randomized clinical trial using RAGT. Subjects trained 2 times per week for 10 weeks for a total of 20 training sessions. Five subjects with progressive MS have completed the RAGT protocol. Four women and one man ranging in age from 33 to 63. The group has a range of EDSS scores from 4.5 to 6.5. Physical Therapists individualized training intensity and RAGT characteristics to maximize benefits for each subject. Motor capacity outcomes (Walking speed and endurance [2 MWT]) and quality of life measures (Modified Fatigue Impact Scale [MFIS] and the Multiple Sclerosis Impact Scale 29 [MSIS-29]) were assessed at baseline and after the final training session (20^{th} session). Subjects were monitored at each visit for adverse events.

Results: There was no reported adverse event for any subject. Three of the five subjects experienced a 10% or greater increase in walking speed with an average improvement of 0.062 m/s. The group averaged 13% improvement in fast walking speed. Subjects experienced an average improvement of 10% on the MFIS and 15% on the MSIS-29. MFIS subscales revealed the greatest amount of improvement in the physical domain (44%). The MSIS-29 subscales indicated that individuals had a significant decrease in physical disability (18%).

Conclusions: These five subjects with progressive MS tolerated the treatment dosage of 2 times per week for 20 weeks and did not experience any adverse event throughout the robotic training. Focused gait training using RAGT resulted in improvement in walking speed. Subjects reported that training reduced their disability and fatigue enhancing their overall quality of life.

Disclosure: *Nothing to disclose.*

Keywords: Complementary/alternative therapies in MS, Equipment in MS, TYPE NEW KEYWORD HERE

(REH27)

Strategies to Foster Buy-in for Physical and Occupational Therapists: Engagement across Multiple Sites and States for a Study on Tele-Exercise and Multiple Sclerosis (TEAMS)

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Background: Tele-Exercise and Multiple Sclerosis (TEAMS) is a research project funded by the Patient-Centered Outcomes Research Institute (PCORI) that aims to deliver a 12-week exercise-based rehabilitation intervention to 820 people with multiple sclerosis (MS) who live in Alabama, Mississippi, and Tennessee. Participants are randomized into one of two study arms: TeleCAM and DirectCAM. The TeleCAM consists of 4 testing visits with the intervention delivered via videos accessible through a tablet app. The DirectCAM arm involves 4 testing visits and 20 clinic visits where the intervention is delivered. Physical and occupational therapists at 43 outpatient clinics across the three states are trained to deliver the intervention to enrolled participants. This researcher-provider model is an integral part of the study design and is critical to the sustainability and success of the project.

Objectives: The **purpose** of this presentation is to describe a multi-tiered approach used to facilitate therapist engagement and form partnerships between the therapists, researchers and study participants.

Methods: A Therapist Manual of Operating Procedures (T-MOP) was developed for each clinic to ensure consistency of intervention delivery. The Clinical Research Coordinator used the TMOP along with a rehabilitation guideline established by the Consortium for Multiple Sclerosis Centers (CMSC) to train clinicians at each clinic. Continuing Education Units (CEUs) were approved allowing each clinician to claim 4 to 6 hours for on-site training. Videos were created to provide an instructional guide on how to administer each outcome measure. *GoToMeeting* was used as a platform to deliver ongoing study updates. Information pertaining to participants is communicated through a HIPPA-compliant portal (*Box*).

Results: 43 clinics across the 3 states and 86 therapists were trained for the study. Each clinic has a copy of the comprehensive (81 pp) T-MOP available in print form with access to a digital

copy on Box. 18 GoToMeetings have been held and recorded for training and study updates, and each of the 86 trained therapists has utilized the outcome measure videos. 43 therapists have access to Box and have uploaded approximately 1900 documents within 26 months. There are 823 participants enrolled in the study and 731 have been baseline tested.

Conclusions: Our implementation science researcher-provider model has established partnerships with therapists, research staff, and participants and has resulted in seamless communications in intervention delivery and data management across the participating clinics in 3 states. Investments in training and engagement of therapists should be considered critical to recruitment, enrollment, retention and dissemination in research. The model can be adapted for other similar projects that require strong emphasis on researchers engaging clinicians in implementation science.

Disclosure: *Nothing to disclose.*

Keywords: Comprehensive care and MS, Engagement , MS and the caregiver/family

(REH28)

Correlates of Change in First Trial Exposures across Two Days of Protective Steps Among Those with MS

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Background: : Multiple sclerosis (MS) is a common, debilitating, neurogenerative disorder that causes myriad symptoms. Gait and balance dysfunctions are common and manifest early in the disease, increasing fall risk. In particular, the ability to quickly and effectively react to a loss of balance is worse in people with MS. Therefore, improving reactive balance among those with MS is desirable. However, for maximum ecological validity, improvements in reactive balance through training would be demonstrable upon *first loss-of-balance exposure*.

Objectives: The aim of this study is to evaluate first trial changes in people with MS before and after one day of protective stepping practice. The study also seeks to identify clinical correlates of first trial changes to begin evaluating for whom such training may provide benefit.

Methods: Fourteen people with MS underwent two, consecutive days of support-surface perturbations using an instrumented treadmill. Protective stepping outcomes were step length, step latency, and margin of stability. The backward step performance on the first trials on days one and two were compared, and difference scores were evaluated for relationships with correlates based on theoretical considerations.

Results: There were no significant changes in first trial performance after training. However, some clinical and cognitive characteristics, such as mini-BESTest performance, improvement from day one to day two on the Symbol-Digits Modality test, type of MS diagnosis, and falls history were related with the amount of change individuals experienced.

Conclusions: Although preliminary, these findings provide evidence that those with more favorable disease states may see more robust first-trial improvements after perturbation training. Greater doses, larger and more homogeneous samples, or longer delay between training and reassessment may be needed to understand the existence and relevance of first trial changes.

Disclosure: *Nothing to disclose.*

Keywords: Rehabilitation

(REH28)

Lifestyle Redesign(R) for Multiple Sclerosis: A Case Series of Female Hispanic Patients

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Background: Research indicates that the incidence rate and clinical presentation of MS varies between patients of different ethnic backgrounds. On average, the incidence rate of Hispanic patients with MS tends to be lower than non-Hispanic whites, while the average age of first reported MS symptom is earlier in the Hispanic population. Hispanic patients have higher incidence of cervical spinal lesions, mobility impairments, and optic neuritis at first MS-related event. Patients with MS of Hispanic descent may be at a higher risk of disability earlier in the disease process. Due to the identified clinical presentation and disability risks, it is critical to provide rehabilitation services that will support symptom and disease management.

Evidence in the MS literature supports behavior and lifestyle interventions as critical components for symptom and disease management, as well as improved quality of life. Lifestyle Redesign(R) is an occupational therapy (OT) approach that focuses on helping patients acquire health-promoting habits and routines to improve overall function, health, and quality of life, as well as to improve self-management of chronic conditions. This methodology involves education, occupational self-analysis, personal exploration, and goal setting interventions, in order to facilitate reflection, and increase motivation for and the enactment of health-promoting behavior changes.

Objectives: Describe the delivery of Lifestyle Redesign(R) to address chronic disease and symptom management in patients with MS within an OT plan of care and provide a descriptive case series with clinical outcomes to demonstrate how this intervention can be applied clinically with Hispanic females with MS.

Methods: The subjects included in this case series participated in an average of 11 OT sessions. All subjects are female, of Hispanic descent, and between the ages of 20 and 45. The Canadian Occupational Performance Measure (COPM), Multiple Sclerosis Quality of Life Inventory (MSQLI), and Health Related Quality of Life Short Form-36 (SF-36) were used at pre- and post-intervention.

Results: Clinically significant improvements occurred in the COPM overall performance and satisfaction scores, with patients demonstrating an average 5.3-point increase on performance and an average 7.2-point increase on satisfaction. On average, SF-36 scores improved in seven subscales including emotional well-being, social functioning, and bodily pain, and MSQLI scores improved in three subscales including the MFIS.

Conclusions: This case series supports the use of Lifestyle Redesign(R) to address symptom and chronic disease management in Hispanic females with MS due to the demonstrated benefits in the areas of functional performance and symptom presentation. Additionally, this case series contributes to the broader evidence for the feasibility of Lifestyle Redesign(R) services for neurological populations.

Disclosure: *Nothing to disclose.*

Keywords: Comprehensive care and MS, Lifestyle interventions, Management of activities of daily living in MS

(REH29)

Cognitive Processing Speed As a Predictor of Motor Skill Learning in Healthy Adults and Persons with Multiple Sclerosis

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Background: Motor and cognitive deficits are frequently reported in individuals with Multiple Sclerosis (MS), resulting in a high incidence of rehabilitation enrollment. Presently, there is no way to predict whether a patient will benefit from a specific rehabilitation program and factors mediating exercise responsiveness in MS remain unknown.

Objectives: This study aims to determine baseline cognitive and pathological predictors of an individual's ability to benefit from a balance-training program. We hypothesized that faster

processing speed and increased myelin water fraction (MWF) in brain regions related to balance at baseline would result in greater automaticity at the trained task, as measured by the change in Dual-Task Cost (DTC) following training.

Methods: 4 healthy participants and 1 MS participant (1 Male, 4 Female; age 40± 14.3 year) underwent an MRI examination and 4 consecutive days of balance training on the Neurocom Basic Balance Master. Each day involved a single session of 20, 2-minute blocks; participants performed weight shifts on a force platform in response to targets on a screen. Participants were evaluated pre- and post-training on their ability to perform a dual-task (Limit of Stability Test + N-back Test).

Results: Following training, all participants demonstrated improvements in reaction time (14%), velocity (34%), directional control (5%) and target accuracy (6%) on the challenging balance task. Reductions in DTC were seen across individuals, suggesting lower extremity motor skill training is feasible. Faster baseline processing speed on the Symbol Digit Modalities Test predicted reduced motor DTC in velocity (r= 0.671), 95% CI [-1.00, 0.00] and directional control (r=0.783), [0.11,1.00] following training. Lastly, MWF values across brain regions related to balance were lower in the MS participant compared to age-matched healthy controls.

Conclusions: Data collection is ongoing; processing speed holds promise as a baseline indicator of the ability to benefit from a motor learning paradigm targeting postural control and balance. Given that demyelination is the pathological hallmark of MS, and the MWF of the participant with MS is lower, our myelin water imaging data displays feasibility to distinguish myelin-specific changes that may reflect exercise responsiveness. Identifying key variables associated with successful recovery of motor skills is a promising driving-force for improvements in field of neurorehabilitation.

Disclosure: *Nothing to disclose.*

Keywords: Imaging and MS, Rehabilitation methods

Relapse Therapy

(RTH01)

Safety of Satralizumab Based on Pooled Data from Phase 3 Studies in Patients with Neuromyelitis Optica Spectrum Disorder (NMOSD)

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Background:
Interleukin-6 (IL-6) is implicated in the immunopathology of neuromyelitis optica spectrum disorder (NMOSD). Satralizumab, a humanized recycling monoclonal antibody that binds to the IL-6 receptor, demonstrated a reduction in NMOSD relapse risk in two phase 3 studies: SAkuraSky (satralizumab in combination with baseline immunosuppressants; NCT02028884), and SAkuraStar (satralizumab monotherapy; NCT02073279).

Objectives:
To evaluate the safety of satralizumab vs placebo in a pooled population of patients with NMOSD from the SAkura studies, using the latest data from studies' open-label extension (OLE) periods.

Methods:
SAkuraStar and SAkuraSky are randomized studies comprising a double-blind (DB) period (satralizumab 120mg Q4W vs placebo) followed by an open-label extension period (satralizumab only). The combined DB and extension period was defined as the overall satralizumab treatment (OST) period (cut-off 7 June 2019). Safety was evaluated in the DB and OST periods and reported as adverse event (AE) rates per 100 patient-years (PY).

Results:
The pooled DB population included 178 patients (satralizumab, n=104; placebo, n=74), and a total of 166 patients received satralizumab in the OLE. Mean and median satralizumab exposures in the OST period were 133.3 and 128.6 weeks. Rates of AEs and serious AEs were comparable between satralizumab and placebo groups in the DB period (AEs: 478.49 vs 506.51 events/100PY, respectively; serious AEs: 14.97 vs 17.98 events/100PY, respectively), and were consistent in the OST period. In the DB period, four patients (3.8%) in the satralizumab group and six (8.1%) in the placebo group withdrew from study due to an AE. Infection rates were lower with satralizumab vs placebo in the DB period (113.04 vs 154.85 events/100PY), with no increased risk of opportunistic infections. Infection rates with satralizumab were similar between the DB and OST periods. The injection-related reaction (IRR) rate was higher with satralizumab vs placebo in the DB period (17.03 vs 8.99 events/100PY); IRRs were mostly mild-to-moderate and did not lead to treatment discontinuation. No deaths or anaphylactic reactions were reported.

Conclusions:
In patients with NMOSD, satralizumab was well tolerated and showed a favourable safety profile. Results from the overall satralizumab treatment period, which expanded on the DB periods by adding data from the ongoing OLE periods, were consistent with the DB period results.

Disclosure: *Benjamin M. Greenberg: Abcam, Alexion, EMD Serono, Genetech, Novartis (consulting fee). Chugai, CLENE Nanomedicine, Guthy Jackson Charitable Foundation for NMO, Medimmune, NMSS, PCORI, Transverse Myelitis Association (contracted research). Jerome de Seze: Chugai, Roche (consulting fee). Edward Fox: Abbvie, Biogen, Celgene, EMD Serono, Sanofi Genzyme (personal fees and grants). Chugai (contracted research, personal fees and grants, personal fees and non-financial support – recruiting site for the sakurastar study). Genetech, MedDay, Novartis, Roche, TG Therapeutics (consulting fee, contracted research, speakers bureau). Albert Saiz: Bayer-Schering, Biogen, Merck, Novartis, Roche, Sanofi, Teva (speakers bureau). Takashi Yamamura: Alexion Pharma, Ono (consulting fee). Biogen, Novartis, Teijin Pharma (consulting fee, speakers bureau). Chiome Bioscience, Miraca Holdings (contracted research). Chugai (consulting fee, contracted research, grant, speakers bureau). CSL Behring, Mitsubishi Tanabe, Takeda, Teijin Home Healthcare (speakers bureau). Carole Marcillat, Xiujing Kou, Kristina Weber: F. Hoffmann-La Roche (salary). Brian G. Weinshenker: Alexion, Chugai, Mitsubishi Tanabe, Roche, Viela Bio (consulting fee). Hospices Civil de Lyon, MVZ Labor PD Dr Volkmann und Kollegen GbR, Oxford University, RSR Ltd (royalties).*

Keywords: Neuromyelitis optica spectrum disorder

(RTH02)

Adolescents with Nmosd Achieved Similar Exposures and Favorable Safety Profile When Treated with the Adult Satralizumab Dosing Regimen

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Background:
Interleukin-6 (IL-6) is implicated in the immunopathology of neuromyelitis optica spectrum disorder (NMOSD). Satralizumab, a humanized recycling monoclonal antibody that binds to the IL-6 receptor (IL-6R), demonstrated a reduction in NMOSD relapse risk in two phase 3 studies: SAkuraSky (satralizumab in combination with baseline immunosuppressants; NCT02028884) and SAkuraStar (satralizumab monotherapy; NCT02073279).

Objectives:
To describe satralizumab exposure in adolescents with NMOSD to support dose selection.

Methods:
Patients in both studies (N=178) received placebo or satralizumab 120 mg at Weeks 0, 2 and 4, and every four weeks (Q4W) thereafter. Data on clinical and protocol-defined relapses (PDRs), aquaporin-4 autoantibody (AQP4-IgG) serostatus, safety endpoints, and pharmacokinetic (PK) and pharmacodynamic (PD) markers were evaluated in adolescent patients. A popPK model,

developed using data from a Phase I satralizumab trial (healthy volunteers) and both Phase 3 studies, was used to analyse PK data.

Results:
Eight adolescent patients were enrolled in SAkuraSky (adolescents were not permitted in SAkuraStar). Seven were evaluated for efficacy (one patient had PK data only). The mean age was 15.4 years (range 13-17); mean weight (79.3kg [range 47.5-140.4]) was similar to the adult population. Six patients were female; three patients were AQP4-IgG seropositive.

The range of model-predicted exposures was similar to those in adults, correlating inversely with body weight, and not age. Treatment effects on soluble IL-6R levels, a marker of target engagement, were similar between adults and adolescents, with similar predicted median IL-6R occupancy (>95% maintained over the dose interval). One of four patients receiving satralizumab experienced a relapse (PDR, n=1); all three patients receiving placebo relapsed (PDR, n=1; clinical relapse, n=2). The safety profile of satralizumab in adolescents was consistent with the adult patient population; no new safety signals were identified.

Conclusions:
These findings support the recommendation that adolescent patients with NMOSD receive the adult 120 mg loading and Q4W maintenance regimen of satralizumab.

Disclosure: *Cheryl Hemingway: Biogen, Roche (consulting fee). Novartis (consulting fee, speakers bureau). Hanna Silber Baumann: F. Hoffmann-La Roche, Innovation Center (salary). Xiujing Kou, Patricia Sanwald Ducray, H.-Christian von Buedingen: F. Hoffmann-La Roche (salary). Daniela Stokmaier: Roche (salary). Veronica G. Anania: Genentech (salary). Hajime Ito: Chugai (salary). Sian Lennon-Chrimes: Roche Products LTD (salary).*

Keywords: Neuromyelitis optica spectrum disorder

(RTH03)

Efficacy and Safety Outcomes from a Prospective Observational Registry of Repository Corticotropin Injection for Relapse of Multiple Sclerosis

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Background: Effective relapse treatment is critical for minimizing disability in patients with multiple sclerosis (MS). Repository corticotropin injection (RCI) is approved by the US Food and Drug Administration for the treatment of MS exacerbations.

Objectives: This multicenter, prospective, observational registry study aimed to characterize treatment response, recovery, and safety outcomes of RCI in the treatment of acute MS relapse.

Methods: The following data were obtained upon initiation of RCI therapy (baseline) and again at various time points after. Clinical outcomes were assessed using the MS Impact Scale (MSIS-29v1), Expanded Disability Status Scale (EDSS), and Clinical Global Impression of Improvement (CGI-I) scale. Patient-reported outcomes were collected via the Work Productivity and Activity Impairment Questionnaire: MS (WPAI:MS) and Health Resource Utilization (HRU) questionnaire. Mean changes from baseline were evaluated at 2 and 6 months via 2-sided paired t tests. Serious and non-serious adverse events (SAEs/AEs) were reported throughout the study.

Results: After treatment with RCI (N=125), mean MSIS-29v1 physical subscale scores (primary endpoint) decreased from baseline (55.69) at 2 months (−7.99, p=0.0002) and 6 months (−9.64, p<0.0001). Post hoc analyses showed larger improvements in patients who received >5 doses of RCI (n=23) vs. ≤5 doses (n=71) at 2 months (−10.74, p=0.0180 vs. −6.48, p=0.0177) and 6 months (−14.62, p=0.0415 vs. −7.90, p=0.0011). Mean EDSS scores decreased from baseline (3.92) at 2 months (−0.37, p<0.0001) and 6 months (−0.45, p<0.0001), with greater improvement in patients who received >5 doses vs. ≤5 doses at 2 months (−0.50, p=0.0068 vs. −0.24, p=0.0059) and 6 months (−0.64, p=0.0430 vs. −0.36, p=0.0111). CGI-I scores improved in 63.38% of patients (p<0.0001) at 2 months and 61.40% of patients (p<0.0001) at 6 months postbaseline. Eighty-three AEs were reported by 35 patients (28%), and 16 SAEs were reported by 11 patients (8.8%). The most common AEs/SAEs were MS relapse (4% AE, 4% SAE) and urinary tract infection (3.2% AE, 1.6% SAE). WPAI:MS and HRU responses showed improvements from baseline for most endpoints at 2 and 6 months.

Conclusions: Improvements in clinical MS scales and patient-reported measures of MS impact, along with the low incidence of AEs/SAEs, support the efficacy and safety of RCI as a treatment option for MS relapse. Treatment response showed greater improvements with >5 doses.

Disclosure: *Jeffrey Kaplan: Alexion, Allergan, Amgen, Biogen, EMD Serono, Lilly, Teva (speakers bureau). Tamara Miller: Acorda, Amgen, Mallinckrodt Pharmaceuticals, Reven (speaking and consulting fees). Adamas, Elan, EMD Serono, Ipsen, Mallinckrodt Pharmceuticals, ONO, Sun Pharma (contracted research). Allergan, Biogen, Genentech, Novartis, Sanofi-Genzyme, Teva (contracted research, speaking and consulting fees). Matthew Baker: Acorda, Avanir, Biogen, Celgene, Genentech, Mallinckrodt Pharmaceuticals, Sanofi-Genzyme, Teva (consulting fee). Bryan Due, Enxu Zhao: Mallinckrodt Pharmaceuticals (employee).*

Keywords: Comprehensive care and MS, Disease-modifying treatments in MS, Immunology and MS

(RTH04)

A Prospective Clinical Trial Utilizing an Ios Mobile Application and Apple Watch to Manage Multiple Sclerosis and Predict Disease Relapses.

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Background: Multiple Sclerosis (MS) is a chronic neurodegenerative disease caused by the lesion forming demyelination of the Central Nervous System. Relapsing forms of MS are indicative of short periods of new or worsening symptoms, often associated with new lesions or increase demyelination. Early identification of disease relapses is crucial for facilitating earlier treatment and minimizing functional decline. The current standard of care relies on clinic visits at 3, 6, or 12-month intervals to assess a patient's disease status and facilitate necessary treatment. This format may lead to overlooked disease worsening. A new and expanding practice in the field of disease monitoring and treatment is the use of wearable data recording technology. Such technology can monitor physical, cognitive, and emotional status in MS patients in real-time may act as an additional resource in MS treatment.

Objectives: The primary purpose of this study is to test the acceptability and feasibility of the comprehensive mobile app "MS Health Connect" and its integrated wearable technology. Additionally, this study aims to investigate whether relapse indicators or objective evidence of disease progression can be identified and correlated to recorded data. The testing and utilizing of this application aim to assess patient quality of life, MS severity, ambulatory changes, and fall detection.

Methods: Study duration for each patient is one year. Patients will have access to a mobile and apple watch compatible version of the app. Patients are to wear the Apple Watch daily and complete weekly or bi-monthly mood, balance, and health surveys. Weekly 2-minute walk tests are also required. Walk tests are performed remotely utilizing the inherent watch features. At baseline and every three months after on-boarding, patients have a scheduled appointment in which patients will complete cognitive, visual acuity, dexterity, and physical tests as well as complete quality of life and MS related surveys. Statistical analysis will be conducted for the validity of application components, the correlation of disease progression and Apple Watch recorded data, and additional experimental aims related to the acceptability and feasibility of the app.

Results: To date, 5 patients enrolled. Data is being collected. Further analysis is required.

Conclusions: Positive feedback about the app and its components had been reported. Analysis of completed data is required for any conclusion to be supported.

Disclosure: *Mary Ann Picone: Biogen Inc. (speakers bureau).*

Keywords: Complementary/alternative therapies in MS, Management of activities of daily living in MS, Wearable technology in MS

(RTH05)

Characterisation of the PK and PD of Satralizumab, a Recycling Antibody, to Support Q4W Dosing in Patients with Nmosd

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Background:
Interleukin-6 (IL-6) has been implicated in the immunopathology of neuromyelitis optica spectrum disorder (NMOSD). Satralizumab is a subcutaneously administered monoclonal antibody that binds to and blocks the IL-6 receptor (IL-6R). Satralizumab was engineered to be recycled back into circulation via the neonatal Fc receptor (FcRn), increasing its serum half-life and effecting prolonged inhibition of IL-6R signalling.

Objectives:
To define an effective, convenient, long-term dosing regimen for satralizumab in patients with NMOSD.

Methods:
The pharmacological characteristics (pharmacokinetics [PK] and pharmacodynamics [PD]) of satralizumab were assessed in 72 Japanese healthy volunteers (HVs; single dose, range 30-240 mg), 33 rheumatoid arthritis (RA) patients (multiple doses, range 30-120 mg), and 104 NMOSD patients from two phase 3 studies in NMOSD (SAkuraSky [NCT02028884] and SAkuraStar [NCT02073279]; 120 mg loading, once every four weeks [Q4W]). A popPK model, based on HV and NMOSD data, was used to derive predictions for individual PK parameters.

Results:
Satralizumab provided significant inhibition of IL-6R signaling for 4 weeks; target engagement resulted in sustained increases in soluble IL-6R levels in HVs, RA and NMOSD patients. In the NMOSD population, the PK of satralizumab was shown to be non-linear, with an effective half-life of approximately 30 days at a dose of 120 mg; the median predicted IL-6R occupancy was maintained at >95% throughout the 4-week dose interval. Meaningful and comparable efficacy vs placebo was demonstrated in patients with NMOSD in both phase 3 studies: hazard ratio (95% CI) for reduction in protocol-defined relapse risk was 0.38 (0.16-0.88), p=0.0184 in SAkuraSky; and 0.45 (0.23-0.89), p=0.0184 in SAkuraStar). Satralizumab showed a favorable safety profile in patients with NMOSD when administered as monotherapy or in combination with baseline immunosuppressants.

Conclusions:
The recommended 120mg loading and Q4W maintenance regimen of satralizumab represents an effective, safe and convenient treatment in NMOSD.

Disclosure: *Sian Lennon-Chrimes: Roche Products LTD (salary). Hanna Silber Baumann: F. Hoffmann-La Roche, Innovation Center (salary). Gaelle Klingelschmitt, Xiujing Kou, Patricia Sanwald Ducray, H.-Christian von Buedingen: F. Hoffmann-La Roche (salary). Veronica G. Anania: Genentech (salary). Hajime Ito: Chugai (salary).*

Keywords: Neuromyelitis optica spectrum disorder

Self-care

(SEL01)

Understanding Gaps in Knowledge Surrounding Flu Shots & Immunizations As They Relate to MS

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Background: Over the past five years the influx of FDA-approved treatment therapies, and advances in symptom management for multiple sclerosis has been astounding. Emphasis has been placed on a healthy lifestyle to maximize quality of life and many experts including the AAN and the CDC agree that receiving vaccinations and flu shots are a part of staying healthy, including for most individuals living with MS. However, this evolving landscape in care and treatment options has also heightened questions, misconceptions, and confusion surrounding the influence of flu shots and immunizations on MS.

Objectives: Seeking to better understand gaps in knoweldege and what MS patients know/believe about flu shots and immunizations this assessment sought to analyze: 1) key areas of concern for receiving flu shots or immunizations; 2) how flu shots and immunizations are discussed with HCP's; and 3) understand current beliefs surrounding flu shots and immunizations.

Methods: MSAA developed and disseminated a 27-question survey on the topic of flu and immunizations as they relate to MS patients that was emailed out to the MSAA client database.

Results: 1,926 MS patients participated in the survey with 32% of respondents reporting that they do not receive an annual flu shot and do not anticipate getting one this year. When asked why respondents do not receive flu shots 36% opted concerns that flu shots are not good for people with MS; 32% are worried about side effects; and 28% do not trust or believe them to be safe. 68.26% reported an MS Neurologist as their leading source of information, but still 37.74% said that they do not feel well informed about flu shots and 36.28% do not feel well informed enough about immunizations. 42% of respondents feel worried that if they receive an immunization or flu shot, they will have an adverse reaction and 38% believe that if they receive an immunization or flu shot it will interfere with their disease modifying therapy or worsen their

MS. Overall, 62.19% of individuals feel well informed about flu shots and immunizations while 37.81% feel that they need more information.

Conclusions: These findings suggest that although experts agree that flu shots and immunizations are recommended for most individuals, there is still significant confusion among the MS patient community. “I believe that there are links between flu shots / immunizations and multiple sclerosis”, reflected “not sure” responses of 38.81% and 42.51%, respectively. Finally, when asked how they would prefer to receive information about flu shots and immunizations in the future, leading responses were from their MS Neurologist, General Care Practitioner, and through printed materials.

Disclosure: *Nothing to disclose.*

Keywords: Healthy Lifestyle while Living with MS

(SEL02)

Experimental Project Fashion Design and Social Inclusion: Multiple Women

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Background: Multiple Women is an experimental project composed by an inclusive clothing collection for social ocasions. Through Social Design guidelines, the work embraces textile mechanisms that pursue to aswer the physiological limitations of women with Multiple Esclerosis.

Objectives: To articulate Fashion Design and Social Inclusion among MS, with the purpose to develop garments with ergonomic adaptations.

Methods: A group of 95 women with several types of MS, aged 20 to 40 with EDSS amid 2.0 and 3.0, took part of structured interviews containing 12 questions upon their daily requirements and clothing demands. A graphic and a infographic were elaborated as design visual tools in order to identify their current needs, the definition of the project parameteres and the planning of possible alternatives. Along with a conceptual panel wich associates the disease with textile features and panels of problems and solutions.

Results: From the elucidation of the dificulties with zippers, buttons, closures, lashings and thick fabrics it was unleashed a collection of 6 drawn apparel and 4 manufactured. The clothes presents trespass, tailored zippers and buttons, and lightweight trim wich collaborates with motor

coordination. All of the clothes carry a QR Code that directs the user to an Instagram video that teaches how to wear the collection.

Conclusions: The project proved to be appropriate to help the quality of life, promoting confort, self steem, safety and autonomy in the dressing process. The ergonomic alternatives show results that attend aesthetics and functionality demands that are scarce in the market.The challenge involves the creations in modeling and replacement of materials.

Disclosure: *Nothing to disclose.*

Keywords: Complementary/alternative therapies in MS

(SEL03)

An Assessment of the Feasibility of a Dyadic Physical Activity Intervention for Persons with Advanced Multiple Sclerosis and Their Family Caregivers: Work in Progress

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Background: Many people with MS (PwMS) and their caregivers (CGs) do not engage in sufficient physical activity to achieve important health benefits. Emerging evidence in other disease contexts (i.e., Parkinson's and Alzheimer's disease) suggests that dyadic (i.e., partnered) physical activity interventions may improve health and wellbeing for *both*care-recipients and CGs. In MS, physical activity interventions rarely focus on people with advanced disability or target PwMS-CG dyads. To address this important gap, we have developeda theory-based, manualized, dyadic intervention that incorporates evidence-based strategies for improving physical activity (*Physical Activity Together for PwMS and their CGs* (PAT-MS)). PAT-MS is a 12-week, teleconference-delivered intervention that includes education, guidance and support from a trained activity coach, as well as behaviour change techniques (e.g., dyadic goal setting).

Objectives: To evaluate the feasibility of PAT-MS for people with advanced MS and their CGs.

Methods: A single-site, assessor-blinded, randomized controlled pilot feasibility trial, with 1:1 allocation into an immediate intervention or a delayed control condition. A target of 20 PwMS-CG dyads will be included. PwMS-CG dyads will receive six group teleconferencing sessions (~60mins) every other week for a period of 12 weeks. The group sessions will be interspersed with brief (~15 mins) one-on-one support telephone calls in the weeks that the group sessions do

not occur. Feasibility metrics will include process (e.g., recruitment and retention rates), resource (e.g., monetary costs and communication time), management (e.g., time and accuracy of data collection/entry), and scientific assessment (e.g., safety and participant experience).

Results: Data collection is ongoing. Anticipated completion is March 2020. The main findings regarding intervention feasibility will be presented.

Conclusions: PAT-MS is the first physical activity intervention to target both PwMS who have advanced disability and their CGs as active participants. The intervention presents a unique opportunity to increase physical activity behaviour and improve the health outcomes of both PwMS and their CGs. The findings of this study will provide critical information on feasibility metrics that will inform and refine the design and delivery of subsequent stages of this research.

Disclosure: *Nothing to disclose.*

Keywords: MS and the caregiver/family, physical activity

Symptom Management

(SXM01)

Effect of Nabiximols on Spasticity and Muscle Strength in Patients with Multiple Sclerosis (MS) across 3 Randomized Controlled Trials

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Background: Spasticity is a common feature of MS, especially in patients with long-standing illness. Medications that reduce spasticity may also reduce muscle strength, potentially impairing the ability to walk. Patients who do not respond adequately to conventional antispasticity medications need additional treatment options that improve spasticity without causing weakness.

Objectives: Assess the relationship between changes in spasticity and muscle strength in lower extremities or mobility, using data from 3 RCTs (GWMS0106, GWSP0604, SAVANT) of nabiximols vs placebo in patients with spasticity due to MS inadequately controlled by antispasticity medications.

Methods: Spasticity was evaluated using the Numerical Rating Scale (NRS) in all 3 trials, muscle strength using Motricity Index (MI) in GWMS0106 and GWSP0604 and mobility using timed 10-Meter Walk Test (10MWT) in GWSP0604 and SAVANT. Adjusted mean differences

for change from baseline in outcome measures between nabiximols and placebo are summarized. Pearson correlation analysis was conducted to assess the association between change from baseline in spasticity and change in strength or mobility for nabiximols and placebo groups separately.

Results: This analysis included 184 patients from GWMS0106, 241 from GWSP0604, and 106 from SAVANT. The baseline mean (SD) Expanded Disability Status Scale score was 6.0 (1.42) in GWSP0604 and 5.9 (1.1) in SAVANT. In GWMS0106, nabiximols significantly improved mean NRS spasticity score (-0.52 points [95% CI: -1.029, -0.004]; p=0.048), without significantly affecting the MI for legs (3.86 [-0.06, 7.78]; p=0.054). In GWSP0604, nabiximols significantly improved mean NRS spasticity score from baseline vs placebo (-0.84 [-1.29, -0.40]; p=0.0002), without significantly affecting the MI for legs (0.97 [-1.49, 3.42], p=0.439) or the 10MWT results (-3.34 [-6.95, 0.26]; p=0.069). In SAVANT, nabiximols significantly improved spasticity vs placebo (-1.9 [-2.73, -1.06]; p<0.0001), without significantly affecting the 10MWT results (-1.71 [-3.84, 0.44]; p=0.11). Pearson correlation coefficients were all under ±0.30 (indicating negligible correlation) for the association between change in NRS and MI and for the association between change in NRS and 10MWT, except for the low positive correlation between NRS and 10MWT in the nabiximols group in SAVANT (0.326).

Conclusions: The improvement in spasticity with nabiximols was not accompanied by muscle weakness often observed with antispasticity medications or by a notable change in preferred walking speed.

Disclosure: *Francois Bethoux: Adamas Pharmaceuticals (contracted research). Biogen (speakers bureau). GW Pharma (consulting fee). Springer Publishing (royalty). Kathryn Nichol: Greenwich Biosciences, Inc. (salary). Joanne Wagner: Greenwich Biosciences/GW Pharmaceuticals (salary). Joanne Wagner, Karen Cartwright: GW Pharmaceuticals (ownership interest). Joris Berwaerts, Elizabeth Gardener: GW Pharmaceuticals (salary). Daniel Checketts: GW Research Ltd (salary). Karen Cartwright: plc stock holder (salary).*

Keywords: Complementary/alternative therapies in MS, Comprehensive care and MS, MS symptom management E

(SXM02)

MS Action Plan May be Effective Tool Helping Patients with Acute Change in MS Symptoms

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Biotherapeutics, Portland, OR; [8]Neurology, St Vincent Neuroscience Center, Billings, MT; [9]University of Washington, Seattle, WA; [10]Swenson Healthcare, Tacoma, WA; [11]National Multiple Sclerosis Society, New York, NY

Background: The Greater Northwest Healthcare Provider Council of the National Multiple Sclerosis Society (NMSS) identified a need for MS patients to be educated on what to do when they experience any new or worsening neurologic symptoms. Council members found that many of their MS patients would check themselves into the ER or Urgent Care for symptoms that may have been better treated in the outpatient setting.

Objectives: The objectives of the MS Action Plan are to 1)foster clear communication between patient and provider 2)help patients avoid any undue trips to urgent care or ER, and 3)educate patients on what to look out for and when they need to contact their MS provider team.

Methods: The Healthcare Provider Council started with a document in use at the Virginia Mason MS Center in Seattle and adapted it for all MS providers to use and share with their MS patients to help them better understand their MS symptoms. The Virginia Mason document was adapted from the Asthma Action Plan which is widely used throughout the country. The MS Action Plan was first distributed at the Greater Northwest Regional MS Summit annual professional education program to an audience of 80 MS care providers in March of 2019. Six months later the Healthcare Provider Council created an online survey and distributed it to the Summit attendees to assess how the MS Action Plan is being used by providers and if they were finding it useful and effective.

Results: Twenty providers responded to the survey. Of the respondents, 60% answered that they have used the MS Action Plan in their practice and 87% found it useful. When asked who provides the MS Action Plan to patients, 80% selected "provider" with "RN" being the second most commonly selected answer. The most common way the clinics are using the action plan is in hardcopy handed to patients, followed by placing the MS Action Plan in exam rooms for patients to take.

Conclusions: The MS Action Plan could be an effective tool in helping MS patients better understand their MS symptoms, and feel confident in their decision making around when to be seen and when to wait. It has the potential for reducing the number of unnecessary ER visits and provides the patient with a clear plan of action should their symptoms change or worsen.

Disclosure: *Gloria von Geldern, Piper Paul, Janet Piehl, Jan Shilling, Nicole Lauwers, Kendra Yale, Piper Reynolds: Nothing to disclose. Dennis Dietrich: Adamas (contracted research). Biogen, Novartis (contracted research, speakers bureau). Sanofi (speakers bureau). Ted Brown: EMD Serono, Greenwich Pharmaceuticals (consulting fee). Merck (research grant). Novartis (speakers bureau). Kiren Kresa-Reahl: Atara Biotherapeutics (salary from 6/3/2019 to present: they have a phase 1 ms trial but no medication on the market). Biogen, Celgene, Genzyme, Novartis (speakers bureau). Annette Wundes: AbbVie, Alkermes (contracted research). Biogen (consulting fee, contracted research). Gary Stobbe: Roche (contracted research).*

Keywords: Comprehensive care and MS, MS and the caregiver/family, MS Symptoms

(SXM03)

Intrathecal Baclofen Therapy in Ambulatory and Non-Ambulatory Multiple Sclerosis Patients: A Single Center Experience

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Background: Spasticity is a common cause of disability and diminished quality of life in patients with multiple sclerosis (MS). Intrathecal baclofen therapy (ITB) is an effective treatment option for MS patients with severe spasticity that is refractory to oral drug administration, but there is limited evidence of its long-term efficacy and safety in ambulatory MS patients.

Objectives: This single center, retrospective case series investigates the outcomes of ITB in ambulatory and non-ambulatory MS patients with medically intractable spasticity over a five-year follow-up period.

Methods: Data from the Mellen Center Intrathecal Baclofen Registry were analyzed retrospectively. All patients were diagnosed with MS and underwent an ITB test injection. Baseline demographics were collected along with outcome measures including: Spasm Frequency Scale, Modified Ashworth scale (MAS), hip flexor strength, and walking speed on the Timed 25 Foot Walk. Group comparisons were done using two sample t-test or Wilcoxon rank sum test and logistic regression was used to assess the occurrence of complications.

Results: 170 MS patients underwent ITB infusion system implantation. The aggregate MAS score for the ambulatory cohort (n=87) was significantly reduced from 13.5±6.96 to 4.54±4.18 at 5 years ($p<0.001$) post ITB implantation. Similarly, spasm frequency (0-4 scale) was significantly reduced in ambulatory patients, from 1.71$\pm$0.78 at baseline, to 0.77$\pm$0.94 at 5 years ($p < 0.001$). The average ITB dose was lower for the ambulatory cohort compared to non-ambulatory cohort except at the 5 year follow-up visit. Among ambulatory patients at baseline, 56 (77.8%) were ambulatory at 1 year with no significant change in walking speed (baseline 0.45 m/s±0.30 vs 1 year 0.38 m/s ±0.39 at 1 year, $p = 0.80$). At the five-year follow-up point, 20 (41.7%) patients remained ambulatory with a walking speed of 0.21 m/s±0.37 ($p = 0<0.001$). Longer disease duration (hazard ratio [HR] 1.04; 95% CI 1.01 – 1.07; $p=0.018$), and lower hip flexor strength at baseline (HR 0.40; 95% CI 0.27-0.57; $p< 0.001$) were predictors for transition to non-ambulatory status after ITB implantation. Complications were more common in the

ambulatory ITB group (n=29, 22.1%) compared to non-ambulatory group (n=10, 8.0%) with an odds ratio (OR) 3.30 (95% CI 2.17-5.02; p=0.017).

Conclusions: ITB is an effective therapy for reducing spasticity in ambulatory MS patients without compromising walking speed in the short term though we did observe a higher complication rate in this cohort. This study supports the use of ITB in carefully selected ambulatory patients with MS. Randomized, prospective studies are needed to provide more information on this important subject.

Disclosure: *Justin Abbatemarco, Austin C. Griffin, Noble Jones, Jennifer Hartman, Keith McKee, Zhini Wang, Sean Nagel: Nothing to disclose. Andre Machado: Abbott (consulting fee). Medtronic (fellowship support). Francois Bethoux: Adamas Pharmaceuticals (contracted research). Biogen (speakers bureau). GW (consulting fee). Springer Publishing (royalty).*

Keywords: Intrathecal baclofen, Management of activities of daily living in MS

(SXM05)

Virtual Delivery of Mindfulness-Based Art Therapy (MBAT) to Improve Symptoms Among Adults with Multiple Sclerosis (MS)

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Background:

Stress and fatigue in individuals with multiple sclerosis (MS) have been linked to a more severe course of the disease and weakened immune system. Mindfulness-based interventions (MBIs) have been found to reduce stress and fatigue, and improve quality of life (QOL) in adults with MS. MBIs provided in an online format and led by an multidisciplinary team (nurse & art therapist) might strengthen overall effectiveness of MBIs.

Objectives: The purpose of this pilot study was to compare the effect of virtually delivered meditation and mindfulness-based art therapy (MBAT) on the level of symptoms in a sample of adults with multiple sclerosis (MS). We first beta-tested the protocol in two case subjects and collected feedback to identify areas needing improvement. We then plan to pilot the modified intervention to test feasibility, acceptability, and preliminary efficacy among a different sample of adults with MS.

Methods:

Art therapy and psychoeducation interventions were conducted by an MS nurse and an art therapist. Subjects engaged in mindfulness expressive arts interventions following a MBAT protocol on TEAMS, a video conferencing platform. Two facilitators led the interventions, as well as provided psychoeducational resources and feedback. We then interviewed the subjects to gather perceptions and feedback regarding the effectiveness of MBAT interventions in relieving stress and other symptoms. We also collected saliva cytokines, body temperature, and self-reported data on symptoms, physical function (standing balance, gait speed, minutes of daytime activity), and QOL.

Results:

At present, data analysis is ongoing. However, preliminary anecdotal feedback indicates that patients accept the MBAT interventions as accessible easy to use, and helpful in reducing stress and fatigue. For example, one participant reported that creation of a particular art image enabled her to more effectively communicate the need for change with her spouse in a particular area of her life so that she could better manage her stress levels. Participants have also been responsive to psychoeducational resources given during sessions.

Conclusions: Preliminary findings suggest that a MBAT intervention led by a nurse and art therapist in a virtual format may be an effective method for relieving stress and fatigue in adults with MS. Future larger study is warranted for this important intervention.

Disclosure: *Nothing to disclose.*

Keywords: Management of activities of daily living in MS, Nursing management in MS

(SXM06)

A Pilot Study of Mirabegron (Myrbetriq) and Behavioral Modification Including Pelvic Floor Exercise for Overactive Bladder in Multiple Sclerosis

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Background:

Urinary symptoms, including overactive bladder (OAB), are seen in up to 80% of multiple sclerosis (MS) patients. Most anti-spasmodics for OAB are anticholinergic, which may worsen cognition and constipation in MS. Mirabegron, approved for OAB in the general population, is a B3 adrenergic agonist, so it may be better tolerated in MS patients.

Objectives:

To assess safety, tolerability, and efficacy of mirabegron in treating OAB in MS.

Methods:

Twenty-eight patients with MS and OAB were randomized 1:1 into placebo and treatment arms of this double-blind, placebo-controlled 10-week study.

All patients received pelvic floor exercise training and watched a video about behavioral management of OAB. Patients in the control arm received placebo while the treatment arm received mirabegron (25 mg) with optional up-titration to 50 mg.

Seventy-two-hour voiding diaries were used. The primary outcome measure was the change in OAB Symptom Composite Score (OAB-SCS), which assesses voiding frequency and urgency; higher scores mean worse symptoms. Secondary measures included number and volume of micturition, incontinence episodes, and patient assessments of OAB severity.

Results:

While both groups' scores were lower at final visit than at baseline, the final daily average OAB-SCS for the mirabegron group was 0.47 higher than the placebo group ((95% CI = 0.047, 0.893, p=0.031). Thus, the mirabegron group had a worse primary outcome. On the other hand, for Subject Global Impression, the mirabegron group rated overall bladder control as significantly better relative to placebo group (95%CI = 0.375, 2.381, p=0.009). Trends suggesting treatment-related improvement in other secondary measures favored mirabegron on number of micturitions and incontinence episodes per day, but these and other secondary outcomes did not reach statistical significance.

Adverse events were limited and similar between groups and there were no serious adverse events. Drug adherence was about 95%.

Conclusions:

Mirabegron was safe and well-tolerated in this MS population. Our mixed results do not demonstrate benefit from adding mirabegron to a program of behavior modification for OAB. Patients with MS may have neurological differences from a general OAB population that reduce the responsiveness to beta-3 adrenergic agonists. A larger study population may elucidate the extent of the treatment effect on MS patient bladder function.

Disclosure: *Theodore R. Brown: Abbvie, Adamas, Astelas, Merck (contracted research). EMD Serono, Greenwich Pharma (consulting fee). Novartis (speakers bureau). Virginia I. Simnad: Actelion, Biogen, Celgene, Novartis (contracted research).*

Keywords: Bladder management, Comprehensive care and MS, Nursing management in MS

(SXM07)

The Clinical Spectrum of Mog Antibody Associated Demyelinating Disorders: Three Case-Reports

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Background:

MOG antibody associated disorders are distinct from Multiple Sclerosis (MS) and Neuromyelitis Optica Spectrum Disorder (NMOSD) with positive Aquaporin-4-IgG (AQP4-Ab). The full clinical spectrum of this newly described condition is unknown. In this report we sought to describe clinical and imaging presentations of three MOG antibody seropositive patients.

Objectives:

To present three cases of autoimmune MOG antibody associated demyelination

Methods:

The first case describes a 45 years old female who presented with spasm and pain in lower back with radiation to both legs. Also, she had complaints about muscle spasm, fatigue and tremor in right hand. Five years after the onset of first symptoms she developed left retrobulbar optic neuritis (ON) which responded to IV steroids. MRI confirmed left ON and mild cervical and thoracic spinal cord atrophy. A repeat MRI 24 months later showed a few nonspecific foci of T2/FLAIR signal hyperintensity in the subcortical white matter of the bilateral frontal lobes which was not typical in appearance for MS. MS mimics work up repeated and cell-based immunoassay revealed positivity for anti-MOG antibody with a titer of 1:100 and negativity for AQP4-Ab. She was started on mycophenolate mofetil.

In the second case, a 57 years old male who was previously diagnosed with relapsing MS presented with ON. He was treated with interferon beta-1a, Glatiramer acetate, Teriflunomide and Fingolimod. After 8 years from the onset of MS, the patient developed dysarthria, vertigo, and dysphagia initially treated with IV steroids but did not have a good recovery and repeat MRI showed progression of multiple areas of enhancement in the posterior fossa. So, he was admitted to the hospital and received PLEX, which significantly improved his symptoms. Cell-based immunoassay was positive for anti-MOG antibody with a titer 1:1000. Subsequently his treatment was switched to Rituximab and his symptoms remained stable ever since.

The third patient is a 45 years old female with first presentation as paresthesia and progressive cognitive decline who was diagnosed with Relapsing Remitting Multiple Sclerosis (RRMS) based on MRI and presence of Oligoclonal Band in CSF. She had two major attacks presented as

weakness and numbness in lower extremities and face which dramatically responded to high dose steroids. Her last attack presented as ON that partially improved with IV steroids. MRI indicated several enhancing lesions brain as well as cervical and thoracic spine. Cell-based immunoassay revealed positivity for anti-MOG antibody with a titer 1:100 and negativity for AQP4-Ab. Treatment with Ocrelizumab started afterward.

Results:

Three cases are presented.

Conclusions:

MOG associated demyelinating disorders seems to represents a new disease entity. Reporting MOG seropositive cases helps expanding our knowledge about its clinical and imaging presentations, disease course and the best available treatment options.

Disclosure: *Nothing to disclose.*

Keywords: Myelin oligodendrocyte glycoprotein antibody, MOG antibody associated demyelinating disorder, Cell-based immunoassay, Natural history of MS